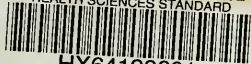


COLUMBIA LIBRARIES OFFSITE
HEALTH SCIENCES STANDARD



HX64128601

RC683 .Ab2

Congenital cardiac d

RECAP

Columbia University
in the City of New York

College of Physicians and Surgeons

Library





Digitized by the Internet Archive
in 2010 with funding from
Open Knowledge Commons

CONGENITAL CARDIAC DISEASE

BY

MAUDE E. ABBOTT, B.A., M.D.

MCGILL UNIVERSITY, MONTREAL, CANADA

REPRINTED FROM
OSLER & McCRAE'S MODERN MEDICINE
Vol. IV, 2d Edition, 1915

LEA & FEBIGER
PHILADELPHIA AND NEW YORK

Thes.

22-34908

RC683

At 2

CHAPTER X.

CONGENITAL CARDIAC DISEASE.¹

By MAUDE E. ABBOTT, M.D.

Definition.—Congenital cardiac disease may be defined as that condition in which, through arrest of development or disease occurring in intra-uterine life, anomalies in the anatomical structure of the heart or great vessels exist, leading to irregularities in the circulation. It is frequently associated with congenital cyanosis and clubbing of the fingers, and constitutes in extreme cases the *morbis cæruleus* of the older writers.

THE DEVELOPMENT OF THE HEART.

It is impossible to approach this subject intelligently without a certain preliminary knowledge of the development of the mammalian heart. A brief statement referring especially to the development of the septa, the involution of the bulbus cordis and sinus venosus, and the disappearance of the primitive aortic arches, is therefore necessary here. For fuller details the reader is referred to the fundamental studies of His² and Born³ and to the recent contributions of Tandler,⁴ Mönckeberg,⁵ and Mall.⁶

The mammalian heart is formed originally of two straight tubes placed independently on either side of the body, which merge together as the ventral cleft closes in and finally fuse, the septum thus formed becoming entirely obliterated before the permanent interventricular septum begins to appear. Meanwhile a twisting of the heart upon its long axes occurs, and it becomes no longer symmetrical, but S-shaped, with the ventricular portion bent forward and downward and the auricular part upward and backward. It now consists of two chambers, a single ventricle forming its anterior and lower part with its bulbus cordis passing upward and to the left and *giving off the aortic trunk from its right angle* (Figs. 16 and 17), and a single auricle with its sinus venosus lying behind and to the left. At this stage it resembles the two-chambered heart of the fish, and is especially interesting in regard to the formation of the bulbus cordis.

¹ This article has been largely rewritten, and curtailed in parts, to permit of the addition of new material, especially under the Development of the Heart, Anomalies of the Pericardium, Dextrocardia, Congenital Rhabdomyoma, Auricular, Ventricular, and Aortic Septal Defects, Deviation of the Aortic Septum, and Patent Ductus Arteriosus. The reader is referred to the earlier edition for the omitted material.

² *Beiträge zur Anatomie des menschlichen Herzens*, Leipzig, 1886.

³ *Beiträge zur Entwicklung des Säugethierherzens*, Arch. f. mikr. anat., 1889, xxxiii.

⁴ *Keibel and Mall's Human Embryology*, 1912, ii, pp. 534–570.

⁵ *Atlas der Herzmissbildungen*, Jena, 1912; also, Verh. d. Deut. Path. Gesell., Marburg, 1913, xvi, p. 228.

⁶ *Am. Jour. Anat.*, 1913, xiv, p. 249.

The auricle next shifts upward, coming to lie above the ventricle, and its auricular appendages develop enormously, pouching forward on either side of the bulbus (Fig. 19). The atrial canal, in which are developing the

FIG. 16

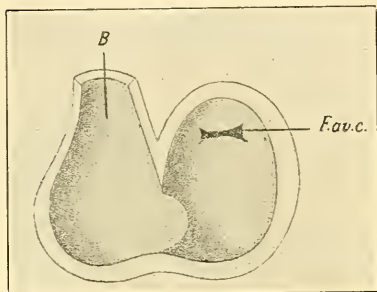


FIG. 17

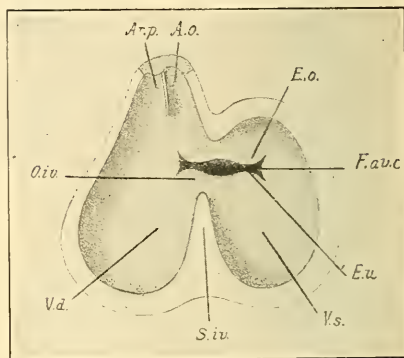
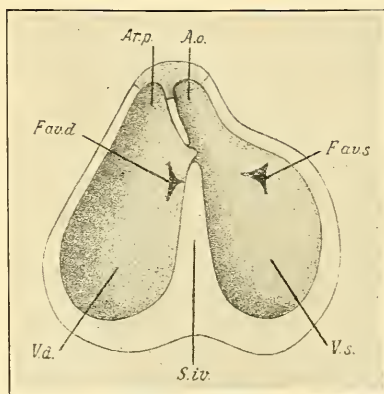


FIG. 18



The separation of the ventricles. (After His.)

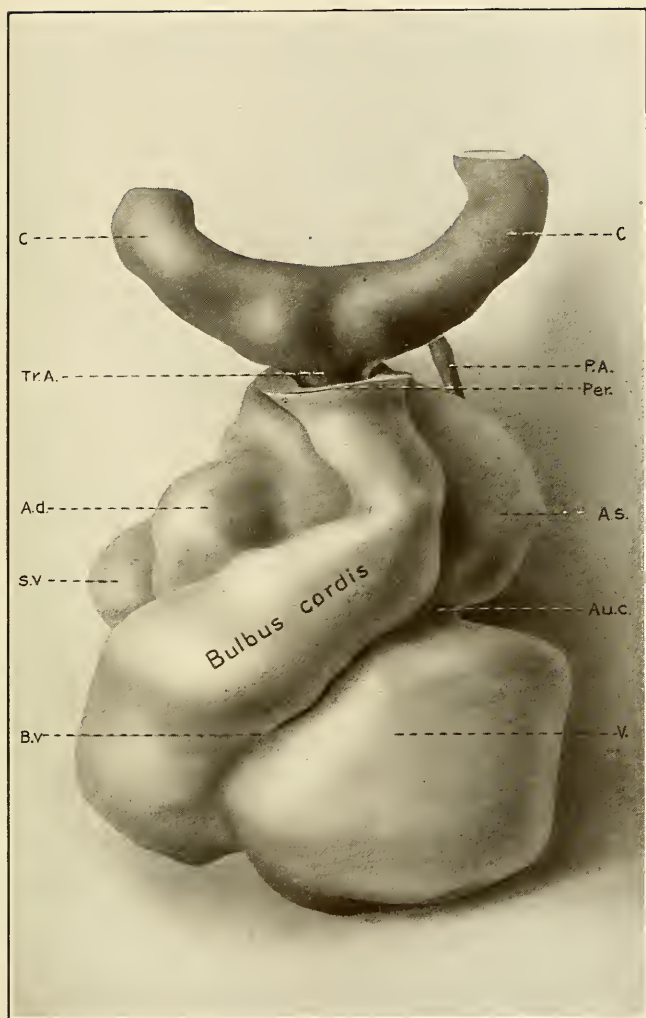
FIG. 16.—Embryo 1.9 mm. long. The single ventricle gives off the common arterial trunk (*B*) from its right upper angle, and receives the common auriculoventricular orifice (*F.au.c.*) entirely on its left side.

FIG. 17.—Embryo 3.5 mm. long. The common trunk has moved somewhat to the left and is divided by the aortic septum. The interventricular septum (*S.iv.*) divides the ventricle into two parts, leaving the interventricular foramen (*O.iv.*) still open above. The auriculoventricular orifice (*F.au.c.*) has moved to the right, so that part of it lies in each cavity. *E.o.*, upper endocardial cushion; *Eu.*, lower endocardial cushion; *V.d.*, right ventricle; *V.s.* left ventricle.

FIG. 18.—The aortic and interventricular septa have united, and completed the division of the ventricles. The pulmonary artery (*Ar.p.*) arises from the right, the aorta (*A.o.*) from the left ventricle, and the right and left auriculoventricular ostia (*F.au.d.*, *F.au.s.*) lie in their respective cavities. *V.d.*, right ventricle; *V.s.*, left ventricle; *S.iv.*, interventricular septum. (From Vierordt, Nothnagel's Series, xv, 1-2.)

endocardial cushions which are to separate the two venous ostia, has become elongated and still opens into the common ventricle entirely on the left side. The sinus venosus is now a separate cavity opening into the auricle on its right wall posteriorly through a narrow cleft, the edges of

PLATE V



Model of the Heart of a Human Embryo 4.6 mm. long x 108.

F. T. Lewis and M. E. Abbott. (Dr. Begg's Embryo.)

(From the Anatomical Laboratory of the Harvard Medical School.)

C., carotid arch; P.A., pulmonary artery; Per., pericardium; Tr.A., truncus arteriosus; A.d., right auricle; A.s., left auricle; S.v., sinus venosus; A.u.c., common auriculoventricular orifice; B.v., bulboventricular cleft; V., common ventricle.

which project into the auricle as the *valvulae venosae dextra et sinistra*. At its upper border it is elongated laterally into the two sinus horns which receive the two superior *venae cavae*, while a single short trunk, the inferior cava, enters it below.

The Bulbus Cordis.—This name is given to a transitory portion of the embryonic heart leading from the right end of the common ventricle to the aortic arches. In the human embryo of 4 to 6 mm. in length the bulbus is a thick-walled muscular tube passing to the left and upward, lined like the rest of the heart with endothelium, which presents certain endocardial thickenings, *spirally arranged* (Tandler), the so-called proximal and distal bulbar swellings, structures which later form the *anlagen* of the semilunar cusps as well as of the lower part of the aortopulmonary septum. In later stages the bulbus disappears, its proximal portion being taken up in the wall of the ventricle, and its distal part, denuded of its musculature and considerably elongated, constituting the primitive aortic trunk. The researches of Greil¹ on the reptilian heart, and Keith,² and recently of Jane Robertson³ on the fish, show that the mammalian bulbus represents what was at one time an independent chamber with muscular walls and its own system of multiple valves, which in the "ontogenetic telescoping of phylogenetic stages" has become submerged.

Robertson correlates her findings in the fish with those of Greil in the lizard, and Born in the mammalian embryo, and traces the bulbus of the latter back through the less blurred stages of the reptile to the simpler forms seen in the Dipnoan and Elasmobranch fishes. Thus this structure, represented in the adult mammal, with its fully established double circulation, by the completely separated aortic and pulmonary trunks, is seen in *Lacerta* (reptile) to consist of a curved muscular tube divided by a spiral aortopulmonary septum, which gives way in turn in *Lepidosiren* (Dipnoan fish) to a kinked muscular tube with median expansion incompletely divided by rows of spirally arranged valves, and this again in the Elasmobranch fishes with their purely branchial respiration, is reduced to the simplest form as a straight channel with muscular walls lined by numerous rows of longitudinally placed valves. These phylogenetic proofs of an early bulbar channel with spiral division of its distal portion, are of the utmost importance in the elucidation of the problems of stenosis of the pulmonary conus and transposition of the arterial trunks, and yield striking confirmation of the explanations offered by Keith of the former, and by Rokitsansky of the latter anomaly.

The Interauricular Septum.—Born showed that the division of the auricles takes place through the development of *two different partitions* placed in planes parallel with each other developing successively, parts of both of which are temporary, while parts persist to form the permanent interauricular septum of postnatal life. Of these septa, the one developing earlier, called by Born the *septum primum*, begins about the fourth week from the upper and posterior wall of the auricle as a sickle-shaped fold which grows forward and downward toward the ventricular cavity, and

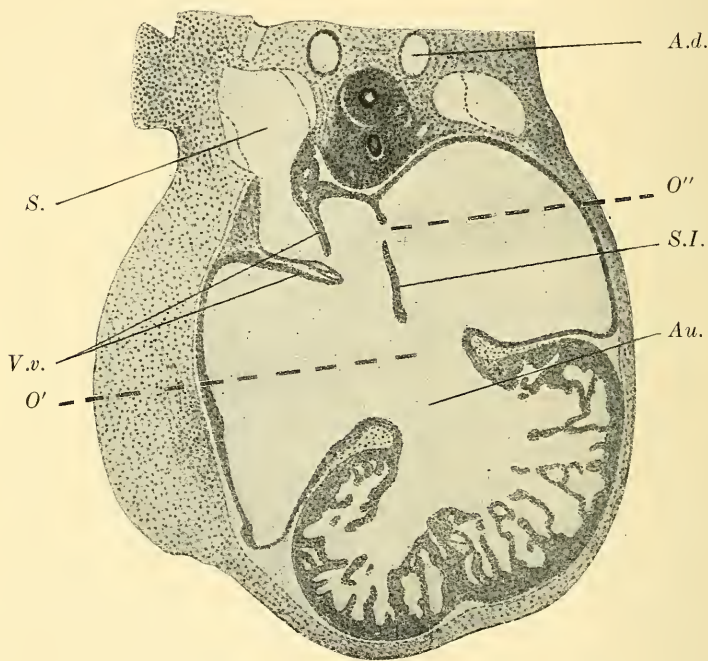
¹ *Morph. Jahrb.*, 1903, xxxi, p. 123.

² *Festschrift of the Quatercentenary of Aberdeen University*, July, 1906.

³ *Jour. Path. and Bacteriol.*, 1913, xviii, p. 191.

for some time an opening exists between the auricles at the lower border of this primitive septum known as the *ostium primum*. About the beginning of the fifth week a second opening, called by Born the *ostium secundum*, forms in the now greatly thinned upper and back part of the septum primum. This second opening grows larger as the ostium primum becomes smaller, and finally disappears entirely (end of fifth week), through the union of the expanded lower margin of the septum primum with the fused endocardial cushions between the auriculoventricular ostia. There thus exists a stage in development when the septum primum is represented by a band of tissue between two orifices, the ostium secundum above, and the ostium primum below. (See Figs. 19 and 20.)

FIG. 19



Transverse section through the heart region of an embryo of 8 mm. greatest length. *A.d.*, descending aorta; *Au.*, atrial canal; *S.*, sinus venosus; *V.v.*, valvulae venosae; *S.I.*, septum primum. Note the bifid apex seen at this stage and also the presence of two openings (*O'* and *O''*) in the primitive auricular septum. In the collection of the I. Anatomical Institute, Vienna. (From Tandler's article in Keibel and Mall's *Embryology*, vol. ii, p. 549.)

The *septum secundum* arises considerably later than the septum primum in a plane a little to its right, from the upper wall of the right auricle, and passes downward covering in the upper and anterior portion of the ostium secundum, thus giving it a valvular character, and transforming it into the foramen ovale of fetal life. A portion of the septum secundum persists in adult life as the *annulus ovalis*, while the *valvula foraminis ovalis* of the adult left auricle represents the remains of the primary septum, the primary and secondary ostia of which have both become obliterated.

The Interventricular Septum.—This begins about the fourth week, just after the origin of the auricular septum, as a crescentic ridge on the inferior wall of the ventricle. It grows upward and backward, its posterior limb merging with the corresponding walls of the ventricle and with the posterior endocardial cushion, and its anterior limb with the antero-ventricular wall along the bulbo-atrial ridges, while its median curved portion unites with a prolongation of the proximal aortic septum (the aortic orifice having moved over from the right to over-ride the ventricular septum), and with the fused endocardial cushions of the auriculoventricular orifice (which has also come to lie in the median line), so that the ventricles are completely separated from each other and the arterial and venous ostia are placed one in either ventricle (Figs. 17 and 18). The point of union of the aortic with the interventricular septum just below the adjacent ends of the anterior and left posterior aortic cusps, remains transparent and devoid of muscle throughout life, and is known as the *pars membranacea*, or undefended space.

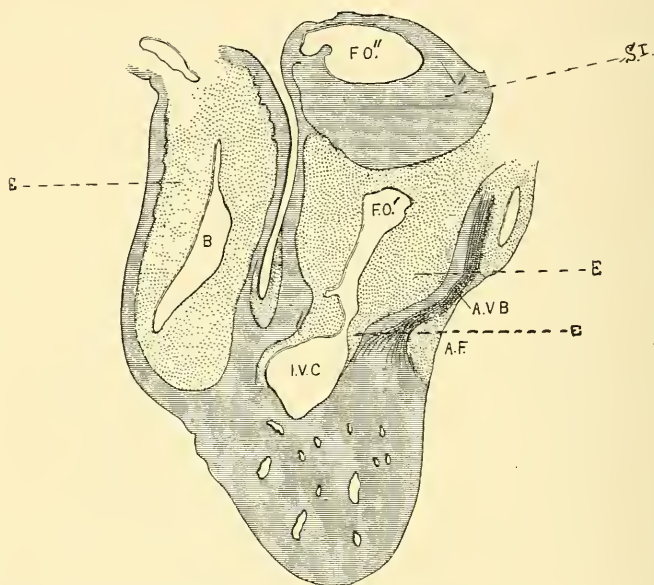
The Aortic Septum.—The *truncus arteriosus* is divided into the two great efferent vessels of the heart by a septum derived from three sources. Before the fifth week a sharp fold, the *aortopulmonary septum proper*, appears in the lumen of the truncus at the point of junction of the 4th and 6th arches (which represent respectively the aortic and pulmonary trunks) and grows rapidly downward. Some distance above the heart this aortopulmonary septum proper meets and fuses with a *spiral septum derived from fusion of the so-called distal and proximal endocardial bulbar swellings*. The bulbus cordis which forms, as stated above, by the involution of its proximal portion the termination of the ventricle, and by the elongation and demuscularization of its distal portion, the first part of the primitive aorta, is supplied internally with a series of endocardial elevations, of which four belong to its distal and two to its proximal part (known respectively as the Distal Bulbar Swellings 1, 2, 3, and 4, and Proximal Bulbar Swellings A and B of Born). These swellings, while symmetrically placed on opposite sides of the tube, have a spiral arrangement from above downward, and the distal swellings 2, and 4, which are much more prominent than the distal swellings 1 and 3, are directly continuous in clock-wise spiral fashion with the proximal swellings A and B. Fusion with each other, first of the more prominent pair of the distal bulbar swellings and later of the proximal ones occurs, the *spiral bulbar septum* resulting, uniting at its distal end with the aortopulmonary septum proper, and the two structures being clearly distinguished from each other by their distinctive histological characters.

The chambers of the heart and the two great arteries have thus been completely separated from each other before the eighth week of fetal life. Meantime, the right horn of the sinus venosus has been taken up in the wall of the right auricle, and the valvula venosa sinistra has disappeared, a portion of the valvula venosa dextra persisting as the *Eustachian valve*, and the left sinus horn remaining as the coronary sinus, while the left duct of Cuvier becomes obliterated (left superior vena cava). The pulmonary veins form later, opening at first as a single trunk, which is later taken up in the wall of the left auricle, thereby enlarging it. The semilunar cusps

appear to form about the seventh week, from the proximal ends of the four distal bulbar swellings, two of which are subdivided in the descent of the septum trunci, so that six cusps, three placed in each artery, result.

The Auriculoventricular Cusps and the Atrioventricular Bundle of His.—The most critical point in the developing heart is undoubtedly the atrial canal. The endocardial cushions, which develop within it, are extensive and vitally important structures, not only as taking the essential part in the formation of the venous ostia, but also as completing the separation of all four chambers by fusion with their respective septa. Moreover, from the observations of Mall on a large series of early human embryos, we learn that the differentiation of the auriculoventricular bundle of His

FIG. 20



Sagittal section through the heart region of an embryo 8 mm. long, $\times 40$, No. 113 of Prof. Franklin P. Mall's collection. *B*, bulbus cordis; *A.V.B.*, auriculoventricular bundle; *A.F.*, annulus fibrosis; *I.V.C.*, interventricular canal; *F.O'*, ostium primum; *F.O''*, ostium secundum; *S.I.*, septum primum; *E*, endocardial cushions. Note the extensive development of the endocardial cushions within the auricle. (From the article by F. P. Mall in the *American Journal of Anatomy*, July 15, 1912.)

is to be traced to the breaking of the continuity of the atrial with the ventricular musculature by the ingrowth of constricting epicardial connective tissue about the external surface of the atrial ring. Thus while in very early stages the muscle of the auricle is continuous with that of the ventricle at all points, in later stages a single band of atrial tissue passing down posteriorly from the lower border of the sinus venosus to the ventricle, and two minor fasciculi on the anterolateral wall, are the only remaining connection between the chambers. The survival of these isolated portions in the general destruction of the muscular continuity between auricle and ventricle is explained by Mall by the anatomical relations of the posterior part of the interventricular septum, which, growing

up toward the posterior endocardial cushion, pushes the epicardial tissue obliquely before it and permits the escape of a small portion of auricular muscle. This surviving atrial tissue, now the only path of conductivity, undergoes differentiation and later, innervation, and becomes readily identified as the auriculoventricular bundle.

This contention of Mall, that the bundle represents persistent atrial tissue, and that its survival at this point is the result of its anatomical relation with the interventricular septum, has received striking confirmation from the investigations of Mönckeberg, and Sato¹ in the distribution of the bundle in various cardiac defects.² Thus in a *Cor Triloculare Bivatriatum* where, in the entire absence of ventricular septum one might conclude a destruction of auricular tissue in the whole circumference of the atrial ring, this bundle was found to be absent from the normal situation and was represented by a small band of tissue accompanying a small vessel on the anterolateral aspect of the heart. In defects of the interventricular septum at the base on the other hand, in which the posterior part of the septum practically always remains entire, the bundle was seen intact in both ventricles, streaming over the lower border of the defect.

The auriculoventricular cusps are formed from the endocardial cushions of the atrial canal. These cushions are a series of elevations of the lining endothelium of the cardiac tube formed by a spongy connective tissue, and are four in number. Two, the anterior and the posterior, develop very early, become of large size, and, growing toward each other, fuse to form the wedge-shaped block which separates the venous ostia and completes the cardiac septa. In addition they encroach by their rapid growth on adjacent structures, so that they come to line the lower border of the *septum primum* in the auricle, while extending also by their apices into the depths of the ventricle. The lateral cushions, of smaller size, develop later, and, with the anteroposterior pair, are converted from endocardial structures into the musculotendinous valves, by the undermining of their substance from without, and by their own invasion of, and fusion with, the spongy musculature of the ventricle.

Primitive Aortic Arches.—After considerable discussion, it is now fairly demonstrated that these number six instead of five, as Rathke described, the disputed fifth arch being rudimentary in character. They are more or less evanescent in all animals, except fishes, in which five persist. In birds and mammals the first, third, and fifth disappear on both sides. In man the fourth left arch becomes the aorta, the fourth right, the right subclavian, while the sixth pair become the pulmonary arteries.

LITERATURE.

The rarity of cardiac defects, the obscurity of their etiology and symptoms, together with the fact that the cases are often of serious clinical import, make the subject of congenital cardiac disease of the highest

¹ Aschoff, *Ber. d. Naturfor. Gesell. zu Freiburg*, December 3, 1913, B. xx.

² Professor Adami informs me that this idea of the persistence of the primitive atrial tissue in the Purkinje fibres of the adult heart was suggested by Gaskell in his book on the *Evolution of the Vertebrates* (1904).

interest. Since the time of Senac¹ it has attracted the interest of many of the ablest workers in the field of cardiac pathology. There are important special contributions from nearly all the earlier writers upon the heart, including Morgagni, Wm. Hunter,² Meckel,³ Louis,⁴ Farre,⁵ Breschet, Sir James Paget,⁶ Gintrac,⁷ Chevers,⁸ and Rokitansky.⁹ The first comprehensive study of the whole subject with a review of this earlier literature, may be said to be Peacock's,¹⁰ which remains a classic and is still the leading authority in English upon the subject. In Germany the ground has been covered by Lebert-Schrötter¹¹ (1879), by Rauchfuss¹² (1878), by Vierordt¹³ (1898), in a statistical study of great value, and more recently by Thorel¹⁴ (1903 and 1911), and Herxheimer¹⁵ (1910). In English there are the excellent general accounts of Humphry,¹⁶ Carpenter,¹⁷ and Keith,¹⁸ and in French the work of Moussois,¹⁹ Gérard,²⁰ and Thérémín,²¹ The last is a study of much value comprising 106 observations of cardiac defects with measurements and illustrative plates.

Perhaps the most valuable and certainly the most brilliant original contribution has been Rokitansky's. This is an analysis of 44 cases of complicated septal defects, together with a study of the normal anatomy of the septa, and of their development as observed by Rokitansky himself, in the human embryo and in the chick. Rokitansky explained all cardiac anomalies associated with septal defects as due to arrest in the development of the cardiac or aortic septa, and to their consequent non-union or irregular union. Although the results of his observations have been modified, his work is of inestimable value as giving a clue to many problems, and especially in regard to transposition of the arterial trunks.

Reference has already been made to the recent work of Keith. From a series of personal observations on conus stenosis, and from the study of 270 malformed hearts in the museums of London, he has advanced the view that cardiac defects are nearly always developmental in origin, that pulmonary stenosis is usually due to subinvolution of the bulbus cordis and that transposition results from an irregularity in involution of the same primitive structure.

¹ *Traité de la structure du cœur, de son action et de ses maladies*, Paris, 1749.

² *Medical Observations and Enquiries*, London, 1784, vol. vi, p. 291.

³ *De Cordis conditionibus abnormibus*, Dissertation, Halle, 1802.

⁴ *Mémoires ou recherches anatomico-pathologiques*, Paris, 1826.

⁵ *On Malformations of the Human Heart*, London, 1814.

⁶ *Edinburgh Medical and Surgical Journal*, 1831, vol. xxxvi, p. 263.

⁷ *Récherches sur la maladie bleue*, Paris, 1824.

⁸ *London Medical Gazette*, series of articles, 1845 to 1851.

⁹ *Defekte der Scheidewände des Herzens*, Vienna, 1875.

¹⁰ *Malformations of the Human Heart*, 1858 and 1866.

¹¹ Article in Ziemssen's *Handbuch der spec. Path. et Ther.*, Leipsic, 1879, Band vi.

¹² In Gerhardt's *Handb. d. Kinderkrankheiten*, 1878, iv, part i.

¹³ *Nothnagel's Spec. Path. u. Therapie*, Bd. xv, 1898. Th. 1., Abt. 11.

¹⁴ *Lubarsch and Ostertag's Ergebnisse*, 1 Abth., 1903, p. 585, and 11 Abth., 1910, p. 268.

¹⁵ *Schwalbe's Missbildungen*, iii Th., iii Lief, 2 Abth., 1910.

¹⁶ *Allbutt's System of Medicine*, vol. iv.

¹⁷ *Brit. Jour. Child. Dis.*, 1909, vol. vi, pp. 337, 385, 433.

¹⁸ *Lancet*, 1909, vol. ii, 359, 433, 519.

¹⁹ *Encyclop. Scient. des aide-mémoires*, Paris.

²⁰ *Rev. de méd.*, 1900, pp. 645 and 837; also *Jour. de l'Anat.*, 1900, pp. 1 and 323.

²¹ *Études sur les affections congénitales du cœur*, Paris, 1895.

The bulk of the literature centres about three questions, which may be stated, with the theories promulgated upon them, as follows:

1. The cause of the defect. Is it developmental or due to intra-uterine disease?

2. The causation of the cyanosis so often present: Is it due to admixture of venous and arterial currents; to delayed aëration of blood; to both these conditions, or to still obscurer causes associated with changes in tissue metabolism and in the composition of the blood itself?

3. In the combination so frequently occurring of defect of the inter-ventricular septum with stenosis of the pulmonary artery, is the septal defect secondary, due to the rise of pressure behind the stenosed orifice before closure of the fetal passages had occurred; or is it primary, the deflection of the current of blood through the defect leading to hypoplasia of the pulmonary artery through disuse? Or are both conditions the result of a common cause, an arrest or deviation or other irregularity in development?

An analysis has been made of the records of 631 cases of congenital cardiac disease which serve here as an illustrative basis. Of these, 205 have been drawn from the *Transactions of the Pathological Society of London*, a few from personal experience, and the remainder from the literature. English and American records have been consulted so far as possible, as these sources are often overlooked in previous statistical studies, which are largely Continental.

ETIOLOGY OF CONGENITAL CARDIAC DISEASE.

Cardiac anomalies may be divided, according to etiology, into two main groups: those due to *arrest of growth* at an early stage, before the different parts of the heart have been entirely formed, and those produced in the more fully developed heart by *fetal disease*.

Arrest of Growth.—From the earliest times search has been made for the underlying causes of the arrest of development manifest in cardiac malformations. Long before Darwin, Meckel, in 1812, pointed out the resemblance of certain defects to the hearts of those animals, which present in a stationary form the different stages through which the mammalian heart passes in its development, and explained them as reversions to a more primitive type.

In seeking the causes of the defect we may turn first to the study of associated anomalies. Do these occur in such frequency and constancy as to place their combination beyond the range of coincidence? And if so, may the causes leading to malformations elsewhere, such as disease and adhesions of the amnion, maternal disease, hereditary predisposition, etc., be assumed to act upon the fetal heart?

In Rokitsansky's *Defekte der Scheidewände des Herzens*, among 24 complicated defects of the septum, all evidently of developmental origin, associated anomalies such as transposition of the viscera, cleft palate, etc., occurred in 8, that is, in one-third of the cases. Vierordt, in the 700 cases reviewed by him, found associated anomalies in 80 (11 per cent.). On the other hand Keith found among 23 malformed fetuses

and infants showing anencephaly, hydrocephaly, spina bifida, umbilical hernia, atresia ani, cleft palate, harelip, and stricture of the œsophagus, in 14 a malformation of the heart.

Among the 631 cases studied here, anomalies elsewhere in the body, among which may be enumerated malformations of liver and lung, asymmetry of calvarium, partial or complete transposition of viscera, harelip and cleft palate, encephalocele, gastro- and rachischisis, absence of spleen or kidney, diverticula, hypospadias, hernia, etc., occurred in 92 cases, that is, in 14 per cent. Defect of the interventricular septum was associated in Chaffey's case with imperforate anus, in Moore's with a supernumerary thumb, in Morestin's with syndactylism and absence of femur, fibula, and genitalia. A widely patent foramen ovale was combined in Berthel's case with rudimentary genitalia, and in Tylecote's with a congenital perforation of the nasal septum. Kingsley reports patent ductus with macroglossia and absence of the left kidney, and Dick a case of pulmonary artery forming the descending aorta, with the uterus bipartite, and the kidneys fused. Mental deficiency or derangement of the higher nerve centres is not infrequent. Thus idiocy was reported by Simmons, Carpenter and Rheiner, in cases of patent foramen ovale, patent ductus, and septal defect respectively, and in a biloculate heart reported by Dublitzhaza, idiocy was combined with strabismus and pes varus.

Further illustrations might be multiplied, but the above suffice to show that the association of grave anomalies with cardiac defects is too frequent to be considered accidental. That the cause of both is to be sought, not so much in a hereditary predisposition, as in a diseased condition of the fetal envelopes or of the maternal tissues is evident from the facts yielded by the family history of these cases. For a history of congenital disease in the ancestry is much less common, than is one of cardiac defect or other anomaly in other members of the same generation, and evidence of infective processes or depressing influences acting within the parental organism is still more frequently supplied. In this series there was a history of congenital defect in a brother or sister of the patient in 11 cases, of rheumatism or heart-disease in the parents in 13, and of small-pox or tuberculosis in six. Congenital syphilis in the father was recorded by Jacobi, in a case of ectopia cordis, and lues whether congenital or acquired is certainly a frequent cause. Baneful influences acting upon the mother during the early weeks of pregnancy have been described, such as great trouble, ill-treatment and fright. Severe inflammation of the bladder of the mother in the third month was blamed by Habershon for the development of pulmonary atresia with septal defect, and an operation on the mother for appendicitis was noted by Royer and Wilson, in their case of incomplete heterotaxy. In not a few instances the parents had both reached advanced middle life, and in some the child was the last of a series of many pregnancies.

Difficult delivery occurred in the cases of patent ductus by Luys, Roeder, and others. Laine reported a case of aortic stenosis with septal defect from a mother aged forty-eight years, who had had four other children, of whom three were feeble-minded.

The predominating cause of the defect is thus clearly to be sought in the immediate environment of the developing embryo. It must be recognized that the early death in most cases of congenital cardiac disease prevents direct transmission of cardiac defects, which might otherwise occur, and this lessens the apparent frequency of heredity. That heredity is a factor in a certain proportion of cases is evidenced by numerous facts. The association of symmetrical polydactylism is significant when one considers the well known familial tendency of this anomaly. Of much interest also is a specimen reported by J. McCrae¹ in which transposition of the viscera and atresia of the pulmonary artery were found in the fifteenth child of a forty-six-year-old mother, who was herself of poor intelligence and had a harelip.

Fetal Disease.—Acute endocarditis was formerly claimed to be a widely acting cause of congenital cardiac disease, not only in those instances in which in the fully formed heart the traces of its presence are incontestable, but in the earlier cases of arrest of growth which were explained as due to its action upon the half-developed embryo. With the increasing knowledge of development, the trend of modern opinion is to explain the majority of cardiac defects as arrest of growth, dependent upon a variety of causes as enumerated above, and to class with these many cases of pulmonary stenosis and atresia, formerly thought to be inflammatory in origin. There remains a certain proportion due to fetal endocarditis, but it is impossible to state the exact degree of its influence, and it is therefore safest to divide cardiac defects into two classes, *viz.*, those in which an arrest of development from any cause has taken place, and those which show, by thickening and cicatricial contraction, that they have been produced by fetal disease after the heart has been fully formed.

The presence of thickening of the endocardium does not prove that a defect is originally due to an inflammatory process, for cardiac defects, giving rise so readily to abnormal currents and to undue strain upon the valves, are particularly liable to be the seat of future disease.

CYANOSIS.

Congenital cyanosis is a bluish discoloration of the skin and mucous membranes, characterizing the more pronounced cases of congenital cardiac disease in which there is serious interference with the circulation. It differs from the cyanosis of the later stages of acquired cardiac lesions in that it may exist for many years without any signs of cardiac insufficiency. Its constant association with the other evidences of deficient oxygenation—dyspnoea and clubbing—raises it almost to the ranks of a disease entity, and such, under the titles *Cyanopathia* or *Morbus Cæruleus*, it was long believed to be.

Pathogenesis.—The immediate causation has long been the subject of debate. It has been variously ascribed to (a) venous stasis, (b) admixture of currents, (c) deficient aëration, (d) dilatation and new for-

¹ *Jour. Anat. and Physiol.*, 1905, xl, 48.

mation of capillaries in peripheral parts of the body, (*e*) changes in the blood itself, *e. g.*, polycythemia. The last two conditions, being subordinate factors and secondary causes only, may be dismissed.

(*a*) The term *venous stasis* is used in this connection to imply obstruction to the free entrance of the blood to the lungs and the resultant back-pressure in the systemic circulation. This theory, advanced by Morgagni, has been largely accepted, but does not explain the situation completely. It is difficult to understand why a simple venous stasis should be sufficient to lead to cyanosis and yet remain unassociated with the œdema and anasarca accompanying back-pressure from other causes. And, on the other hand, the late appearance of the cyanosis in many cases of pulmonary stenosis in which, although the defect has been undoubtedly present at birth, cyanosis only supervenes after some months or years on the occurrence of some event temporarily increasing the embarrassment of the pulmonary circulation renders it evident that some other factor, in addition to the mechanical difficulties which the lesion presents, is, as a rule, needed to bring it about. A highly instructive case is published by Lafitte¹ of a young woman, dying at twenty-one years of a malignant endocarditis, who had always been dyspnoëic on slight exertion but had never presented any trace of cyanosis. At the autopsy the right heart was hypertrophied and about one inch below the pulmonary valves there was a fibrous annular stenosis of the infundibular orifice which was further blocked by large recent vegetations. Peacock, in reporting a case of pulmonary stenosis without cyanosis, suggested that the absence of symptoms was due to the marked hypertrophy of the right ventricle which had succeeded in sending sufficient blood to the lungs for aëration.

(*b*) The theory that cyanosis is due to a *mingling of venous with arterial blood* (wrongly ascribed to Hunter, as Osler points out) has been sharply and apparently successfully refuted by many authorities, notably Peacock. Certain strong arguments can certainly be adduced against its universal application. The classical illustration is Breschet's case, in which the left subclavian arose from the pulmonary artery, and yet the left arm was normal, not discolored. Again, in many instances of biloculate or triloculate heart there is a complete absence of cyanosis. Thus Young² reports a *cor biatriatum triloculare*, both auricles opening into a common ventricle, from which arose the aorta and pulmonary artery, transposed and separated from each other by an anomalous septum in a man, aged thirty-six years, who showed no cyanosis until the last three years of life. Peacock quotes an almost identical case in an infant aged eight months, with only a slight blueness of the lips during dyspnoëic attacks. Equally striking is a case of persistent truncus arteriosus, in which, although the blood from both ventricles entered the common arterial trunk, cyanosis was absent.

The theory of admixture of currents has been revived by Bard and Curtillet³ in a form that has been generally accepted. They describe as *cyanose tardive* a cyanosis occurring as a terminal event, often at

¹ *Bull. de la Soc. Anat.*, 1892, vi, 13.

² *Med. Chron.*, Manchester, 1907-08, xiv, 96.

³ *Rev. de méd.*, December, 1889.

the end of a long life, in cases of patent foramen ovale, when some embarrassment in the pulmonary circulation causes a raised pressure in the right heart leading to a flow of blood through the foramen and sometimes to a forced reopening when it has been closed. They quote an illustration in a man aged fifty-four years, with patent foramen, dying of bronchopneumonia. Long before this, Peacock¹ reported such a case, in a woman, aged twenty-four years, with marked spinal curvature and widely patent foramen ovale, in whom marked cyanosis set in for the first time in the last months of life.

That cyanosis may occur without admixture of currents, in the ordinary application of the term, is definitely shown: (1) by its presence in a limited number of cases of congenital pulmonary stenosis, in which the fetal passages are all closed, and (2) by the fact that the most marked pictures of cyanosis with clubbing may occur in acquired pulmonary emphysema and in bronchiectasis. But in these latter combinations lies perhaps the key to the situation. In bronchiectasis, as Thomas² points out, areas of loss of substance occur, and tortuous dilated capillaries with thickened walls exist, and it is readily conceived that in certain areas blood may pass from pulmonary arterioles to venules without undergoing due oxygenation by the way. In congenital cardiac disease dilatation and thickening of peripheral vessels form a part of the picture, and alterations very similar to those observed in bronchiectasis occur. In a case described by Carpenter³ the lungs were loaded with pigment, their capillaries dilated to three times their normal size, crowded with red cells, elongated, tortuous, their walls thickened and rich in young fibrous tissue elements. Must not many red cells have passed through these thickened channels without receiving their due share of oxygen, and the blood have been thus returned, still largely venous in character, to the left heart. Viewed in this light do not venous stasis and admixture of currents become only a distinction in terms between two conditions leading alike to deficient aëration?

(c) *Changes in the Bloodvessels and Tissues.*—It was suggested by Carpenter that the changes produced in the lungs by the circulation of venous blood might lead to the cyanosis by creating pulmonary obstruction. Certainly a vicious circle is created but the altered capillary circulation, being itself the result of deficient aëration, can be looked upon only as a secondary cause of any symptoms it may help to produce.

(d) *Changes in the Blood Itself.*—The dark color of cyanotic blood has been ascribed to the great increase in red blood corpuscles which often exists. The polycythemia, however, can have no causal relation to the cyanosis, for it not only is not constant in the congenital form, but a very high blood count is consistent with an entire absence of cyanosis, as is evidenced in the polycythemia of high altitudes.

(e) The theory that a variety of causes, including both mingling of currents, venous stasis and pulmonary obstruction, lead to a deficient aëration of the blood and that this is the essential element in the production

¹ *Trans. Path. Soc.*, London, 1859, x, 108.

² *Zeit. f. klin. Med.*, 1901, xli, 58.

³ *St. Thomas Hospital Reports*, 1890, xviii, 285.

of *cyanosis*, is formulated by many recent observers. There is abundant evidence to show that whatever the path by which oxygenation is reduced, whether by direct influx of venous blood into the arterial tree, or by obstruction to the entrance of venous blood into the pulmonary circulation the deficient aëration resulting is in all cases of congenital cyanosis the immediate cause of the symptomatology. The characteristic picture can be traced through the development of the compensatory mechanism of right heart hypertrophy and increased respiratory activity, and polycythemia, to the point where all these processes fail to supplement in the inefficient pulmonary circulation with oxygen sufficient for the body needs. The chronic asphyxia that develops is expressed, not only in the cyanotic hue of the patient, but also in the alterations at the periphery of clubbing and retinal changes. These are the direct results of delayed and toxic tissue metabolism,¹ and an overloaded systemic circulation.

The above considerations may be summarized by saying that the dependence of cyanosis, with its attendant phenomena, upon deficient oxygenation may be accepted as a fact; that the circulation is evidently able to accommodate itself to a certain degree of de-oxygenation, whether this be brought about by obstruction in the course of the pulmonary artery, by a general retardation of flow, or by a mingling of venous with arterial blood, but that as soon as deficient hematosiis reaches a certain limit, oxygenation becomes insufficient for the needs of the body, and cyanosis results. Pulmonary obstruction alone appears capable of producing cyanosis, but it is still a question as to which of the above factors is the essential one, or in what degree they must be combined to bring the circulation to this limit, or what is the amount of venous blood which can circulate without producing symptoms of deficient aëration. That dilated peripheral capillaries, dark color and increased red cell content of the blood, must, when present, add their part to heighten the degree of discoloration is self-evident; but being themselves secondary, these conditions are not to be looked upon as etiological factors, but rather as concomitant effects of a common cause. Lastly, in complicated cardiac defects probably all the factors enumerated combine to produce the mulberry hue and the respiratory distress of the typical *morbus cæruleus*.

Symptoms.—The degree of discoloration varies from a slight bluish tinge of the cheeks and mucous membranes appearing on exertion or excitement, to a distinctly leaden hue of the whole surface, becoming purple in extreme cases. It usually increases gradually, and in many cases marked at the last it is absent at birth, appearing after weeks, months, or even years, when some intercurrent event has heightened the embarrassment in the pulmonary circulation. As a general rule, to which there are a good many exceptions, the degree of cyanosis may be said to depend upon the character of the defect. Thus it is usually *slight* or even entirely *absent*, *except during dyspnœic attacks*, or as a *terminal event*, in *patent foramen ovale*, *patent ductus*, or *septal defects*; a quite *moderate* degree characterizes those anomalies, such as *biloculate* or *triloculate heart*, in which there is a free intermingling of the two blood

¹ *Deut. Arch. f. klin. Med.*, 1910, xcix, 382.

streams, but no pulmonary obstruction; the *marked* cases such as are evident to every casual observer as "congenital heart disease," occur nearly always in *pulmonary stenosis* with or without septal defect; and the most *extreme grades*—the typical "blue baby," are seen in the complete interference with the blood supply to the lungs which takes place in *pulmonary atresia* or *transposition* of the great trunks.

The subject of advanced congenital cyanosis presents a striking appearance. The superficial vessels are often dilated, the face congested, the tongue "geographical," the eyes discolored, and sometimes bulging, the tips of the fingers, toes, and nose, flattened and bulbous, and the respirations heightened to actual dyspnoea. Traces of anasarca and oedema sometimes occur, but form no essential part of the picture, although of course present at the close in cases which terminate with failing compensation. The temperature is usually low, especially in the extremities, and there is a tendency to catarrh, severe coughs, and colds on slight provocation. Hemorrhages, especially from the nose, and spitting of blood are prone to occur. Disturbances of eyesight, dimness of vision or even blindness, may occur from neuroretinitis.

Delayed development is frequent. In Goodman's¹ case, patent ductus arteriosus in a boy aged fourteen, this was evidenced by retarded ossification of the pisiform bone of the wrist on x-ray examination (*Rotch's sign*). The patients are sometimes of very high intelligence, but when the cyanosis has set in early they are often stunted mentally as well as physically, somnolent in thought, and sluggish in action. In females the menstrual function is often delayed in onset, scanty, and irregular. In the cases with marked polycythemia, in addition to peripheral signs of venous congestion and plethora, cyclic (postural or orthostatic) albuminuria may occur. Parkes Weber records a case in a youth aged twenty-two, with great cyanosis and clubbing and a blood-count of 10,300,000 red cells, in whom repeated examination showed the early morning urine to be free from albumin, while that passed at 11 A.M., contained a considerable amount. Cyanotic patients bear the acute infections of childhood well, but frequently succumb to pulmonary tuberculosis. Another common cause of death is broncho-pneumonia.

Special Symptoms.—*Clubbing and Cyanosis Retinæ.*—These symptoms constitute the visible evidences of a generalized dilatation of the smaller bloodvessels over the body surface with accompanying productive changes. New formed capillaries, arterioles with thickened walls, tortuous dilated veins, and new connective tissue formation have been observed in advanced cyanosis, both in the skin (Variot and Gampert²) and in the lungs, as well as in the retina and bulbous finger ends. The causation of these vascular and tissue changes is certainly complex but their chief source is, undoubtedly, stasis and lack of oxygenated blood, and the effect that these conditions produce upon the tissues, by means of the toxic products of metabolism which escape oxygenation.

In *clubbing* of the extremities especially, these mechanotoxic factors are at work, and lead, in extreme cases, to what resembles a congestive

¹ *Amer. Jour. Med., Sc.*, 1911, xxiii, 509.

² *Gaz. d. Hôp.*, vol. xiii, p. 315.

type of scleroderma (Buhl). This is well shown in the cases reported by Ogle,¹ and by Groedel II² of a huge aneurism of the subclavian artery, which, by pressing upon and obliterating the axillary artery and vein and brachial plexus (Ogle's case), led to an enormous tumefaction with intense cyanosis and clubbing, strictly confined to the arm and fingers of the affected side.

Clubbing of pulmonary or hepatic origin, and that of chronic osteoarthropathy (with proliferative changes in the shafts of the long bones), has been sharply distinguished from that of congenital cardiac disease on the ground that there is in the latter cases no new formation of bone (Ebstein³) and that the cause of the clubbing of pulmonary cases is absorption of toxins from the lung. Increased bone formation in the clubbed finger ends of the cardiac cases has been recorded, however, by Bamberger, Janeway,⁴ Groedel II, and Miller.⁵ Further, a case has been reported by Batty Shaw and Cooper⁶ in which in the entire absence of pulmonary disease, signs of septal defect, with deep cyanosis, polycythemia and clubbing were combined with *thickening of the shafts of the tibia and other long bones* as well as of the clubbed terminal phalanges (x-ray examination). This indicates that in this case at least of congenital cyanosis we are dealing with a milder grade of one of the essential symptoms of Marie's disease.

The so-called hippocratic finger ends are broadened laterally and are slightly flattened, of bulbous appearance, with *distally curved nails*, (compare the more elongated finger ends and side to side convexity of the marked pulmonary cases). The nails are often shortened and without lunulæ and may be irregularly thickened from areas of vascularization or thrombotic processes in the matrix below. Microscopically, increase in the soft tissue and often in the fat (deficient aëration) is conspicuous; surprisingly little tissue change is sometimes manifest.

That direct admixture of venous blood is more important in the production of clubbing than pulmonary obstruction alone, is rather strikingly suggested by the fact that in our series, among 40 cases of pulmonary stenosis with open ventricular septum and closed foramen ovale, clubbing occurred in 20, while in 11 cases with closed ventricular septum and open foramen it occurred in 3; and in 7 cases of pulmonary stenosis with septum and foramen both closed, it was not present once.

Cyanosis Retinæ sive Oculi.—Cyanosis of the retina was described and figured in Liebreich's *Atlas*, in 1863. Eighteen published cases were collected by Posey⁷ in 1905, and Holloway⁸ has brought the number recorded to 27. Ocular changes would probably be found in nearly all cases of cyanosis if the eye grounds were examined, and this should always be done for diagnostic reasons; Babinski reported a case in which

¹ *Tr. Path. Soc.*, London, 1859, x, 103.

² *München. med. Wchnschr.*, 1906, liii, 264.

³ *Deutsch. Arch. f. klin. Med.*, 1906, p. 66.

⁴ *Amer. Jour. Med. Sci.*, 1903, cxxvi, 563.

⁵ *Trans. Amer. Ped. Soc.*, 1904, xvi, p. 267.

⁶ *Clin. Soc. Trans.*, 1907, vol. xl, p. 260.

⁷ *Amer. Jour. Med. Sci.*, 1905, cxxx, 415.

⁸ *New York Med. Jour.*, 1912, xiv, p. 71.

dilatation of retinal vessels preceded the appearance of cyanosis; so also Carpenter.

In this condition ophthalmoscopic examination reveals marked changes in the optic disk, congestive and secondarily inflammatory in character. The disk, itself, is unduly reddened or bluish, or sometimes hazy and swollen (neuroretinitis), and is traversed by numerous previously invisible capillaries, and by greatly broadened, often tortuous veins which sometimes show a deep reflex stripe along their surface, and are filled with dark brownish or even blackish-looking blood. The arteries may share in the dilatation and violet discoloration (as in 12 out of the 27 cases recorded), or they may be quite unchanged, showing up in sharp contrast; or again, as in the cases of Baquis and Stanglomeier, they may be contracted. Retinal hemorrhages are common. The difference in the appearance of arteries and veins was suggested by Nagel as diagnostic between anomalies due to admixture of currents (septal defects, etc.), and those due to pulmonary obstruction only, the arteries in the latter case remaining unaltered. This point has yet to be substantiated by postmortem evidence.

In advanced cases the ocular changes are not confined to the disk but involve the whole eye, which bulges outward (exophthalmos) and shows marked conjunctival congestion and cyanosis. Hemorrhages may occur into the vitreous or more superficially, and rupture of the cornea (Goldzieher¹), or glaucoma, from congestion of the ciliary body, may occur. Severe iridocyclitis may develop, as in the cases of Goldzieher and Baquis.² In both of these the iris turned while under observation from a bright blue color to a yellowish brown, a change found by the ocular microscope to be due to extreme congestion. This symptom was the more remarkable because it was seen to disappear after death. Baquis' case was a boy aged eleven, with extreme cyanosis and clubbing, a blood count of 8,500,000 red cells and pulmonary stenosis with septal defect. He gives a careful description of the microscopic findings in the diseased eyeballs and adds a study of eight other cases in the German literature.

Dyspnœa.—Investigation into the respiration of cyanotic cases has been carried out by special methods of precision by Rubow,³ and Bie and Maar.⁴ They show that neither total nor vital capacity is increased, probably because of the hypertrophied heart and dilated veins which commonly occupy so large a part of the thorax, but that the essential compensatory change consists of an increased pulmonary ventilation, by acceleration of the respiratory rate. Dyspnœa is the response made by the centre in the medulla to irritation by the unœrated blood. Peabody⁵ regards it as due to increased acidosis with increased excitability of the respiratory centre. It is a prompt and early feature. It usually sets in before the cyanotic color is manifest. It frequently culminates in the so-called *dyspnœic attacks*, which in their typical form and full develop-

¹ *Centrall. f. prak. Heilkunde*, September, 1904.

² *von Graef's Arch. f. Ophth.*, 1908, lxi, 68.

³ *Deut. Arch. f. klin. Med.*, 1908, xcii, 255.

⁴ *Ibid.*, 1910, xcix, 382.

⁵ *Arch. Int. Med.*, 1914, xiv, 236.

ment, are seizures of extreme respiratory distress usually attended by marked cyanosis, and sometimes by unconsciousness, in which death may take place. Such attacks are characteristic of all severe cases of cyanosis but are frequent also in such conditions as patent ductus arteriosus in which there may be no trace of cyanosis except at these times. Transient cyanosis of this type has been described by Sebilléau¹ as *La Cyanose Paroxystique Congénitale*. Respiratory failure may be evidenced also by repeated syncopes or by anginal crises.

Polycythemia.—This is now well recognized to be a common characteristic of cyanotic blood. The red cells frequently number 7,500,000 to 8,500,000, per cmm. the percentage of hemoglobin is raised, and in some cases the red cells are also increased in size. Counts of 12,750,000 are reported by Murray Leslie,² 10,000,000 by Pick and Parkes Weber, and 9,000,000 by Vaquez and Quiserne.³ Bernstein⁴ reports a case of congenital cyanosis coming on at the sixteenth month, with death at two and one-half years, in which the red cells numbered 10,000,000; the tricuspid orifice was absent and the right heart aplastic with defective interauricular and interventricular septa.

The increase of the red cells is generally thought to be of the nature of a compensatory process, and has been compared to the polycythemia of high altitudes. Weil describes in detail a microscopic finding in two cyanotic children with pulmonary stenosis in whom the red cells numbered respectively 7,502,000 and 8,540,000. The hematopoietic organs and also the other tissues examined were crowded with vasoformative cells and embryonic capillaries and the bone marrow showed a typical erythroblastic reaction. Similar appearances have been noted by other observers and prove that this feature is part of the compensatory mechanism of the organism for the better oxygenation of the tissues.

The blood count differs somewhat at different parts of the body and according to whether the specimen has been drawn from arteries, veins, or capillaries but it remains far above the normal, the increase in red cells remaining an absolute and not a relative quantity (Bie and Maar). That is to say in these cases the total quantity of blood in the vessels is increased, a moderate degree of hydremia existing.

Polycythemia is not a constant feature in congenital cyanosis, it is characteristic rather of the later stages of the disease, and while favorable in so far as it represents an attempt at compensation, its appearance points to a grave prognosis.

Diagnosis.—The cyanosis of congenital cardiac disease must be differentiated from a number of other forms. Of first importance among these is the so-called enterogenous cyanosis⁵ (first described by Stockvis and other Dutch observers), in which the dark color of the blood is due to a

¹ *Thèse de Paris*, 1895.

² *Proc. Royal Soc., Clinical Section*, 1908, i, 34.

³ *Compte rendu de la Soc. de biol.*, July 10, 1904.

⁴ *Ibid.*, 1902, p. 915.

⁵ A digest of enterogenous cyanosis, with a tabulated statement of the recorded cases and full bibliography, is given by West and Clarke (*Lancet*, February 2, 1907). Other important articles are by Hymans van der Bergh (*Deutsch. Archiv f. klin. Med.*, 1905), Oliver (*Lancet*, December 29, 1906), Gibson (*Lancet*, July 14, 1906), and Blackader (*New York Med. Jour.*, March 16, 1907, lxxxv).

sulph-hemoglobinemia or methemoglobinemia, produced, it is thought, by the action of hydrogen sulphide or other toxic agents upon the blood. Again, certain aniline poisons lead to a methemoglobinemia giving a dark discoloration to the skin, and polycythemia with splenomegaly is sometimes, although not always, associated with cyanosis. These conditions differ from congenital cyanosis in the slightly different tinge of the skin, which in methemoglobinemia is of a grayish hue, in polycythemia with splenomegaly of a more florid aspect, by the absence of cardiac signs, by the presence of intestinal symptoms, and by the history of a toxic factor or the presence of enlargement in spleen and liver. In methemoglobinemia the red cells are not increased in number. Other conditions leading to cyanosis with clubbing are pulmonary emphysema, bronchiectasis, and adherent pericardium.

CLASSIFICATION.

Many attempts have been made to reduce cardiac anomalies to a scientific classification, but none have been entirely successful. The most logical arrangement is undoubtedly one based upon the stage of development at which the defect has occurred, differentiating those cases due to arrest of growth from those originating at a period of intra-uterine life and apparently caused by fetal disease. Our knowledge of the development of the heart is still too limited to permit of a complete classification on this basis, and, on the other hand, the etiology of a given condition is often impossible to decide in the individual case. Moreover, a grouping based on development alone is sometimes impractical, for widely different pathological results may ensue from arrest of different parts of the heart at about the same period of fetal life. For these reasons no one classification will be found adequate in its practical application, and it would almost seem that a grouping "on mixed principles" is the only one under which all the cases can be satisfactorily placed.

The 631 cardiac defects here studied present, either as the primary lesion or as a complicating condition, illustrations of practically all the cardiac anomalies known. In the tables¹ of relative frequency, age, sex, etc., pages 342 and 343, an attempt is made to arrange these cases in as logical an order as possible. It represents an attempt at a detailed classification based on strictly anatomical principles and on development so far as this is known, but without regard to the etiology, which is so often obscure. Thus the group of stenosis and atresias of valvular orifices is subdivided, not into inflammatory and developmental forms and their subdivisions, with or without transposition or *rechtslage* (Rauchfuss, Vierordt), but on anatomical considerations only, with regard to the seat of the stenosis and the presence or absence of septal defects.

¹ NOTE.—"Double" indicates a systolic with a diastolic murmur. The sex is not always mentioned in the records of cases. The numbers in these columns do not, therefore, always correspond to the totals in the chart. The data given as to age, sex, postmortem findings, and clinical aspects refer to the cases in the first column in the chart. This column is repeated in the third to last column, and this, added to the second to last column, gives the total relative frequency of each defect, whether classified as primary lesion or as complicating other defects.

STATISTICS OF CONGENITAL CARDIAC DISEASE (631 CASES ANALYZED).

[illegible]

VIII. Defects of aortic septum:
1. Persistent truncus.
2. Defect between A. and P. A.

IX. Transposition of arterial trunks:
1. Complete transposition.
2. Partial transposition.
3. Corrocted transposition
4. Recltstage.

X. Pulmonary stenosis:
1. With closed septa.
2. With patent F. O. closed V. S.
3. With closed P. O. defective V. S.
4. With patent F. O. defective V. S.

XI. Pulmonary atresia:
1. With closed V. S.
2. With closed F. O. defect V. S.
3. With patent F. O. defect V. S.

XII. Pulmonary dilatation:
1. Aortic stenosis and atresia:
1. Subaortic stenosis.
2. Aortic stenosis.
3. Aortic atresia.

XIV. Anomalies of semilunar cusps:
1. Supernumerary cusps.
2. Fusion or defect.

XV. Tricuspid and mitral stenosis and atresia:
1. Tricuspid stenosis.
2. Tricuspid atresia.
3. Mitral stenosis.
4. Mitral atresia.

XVI. Anomalies of aortioventricular cusps:
1. Double orifice.
2. Miscellaneous.

XVII. Patent ductus arteriosus:
1. Simple patency.
2. So-called aneurism.
3. Absence.

XVIII. Anomalous origin.
Coarctation of the aorta:
1. Infantile type.
2. Adult type.

XIX. Hypoplasia of the aorta:
3. P. A. forms descending aorta.

XX. Anomalies of the aortic arch and its main branches:
1. Double aortic arch.
2. Right aortic arch.
3. Anomalous branches.

XXI. Anomalous coronaries:
5. 65

XXII. Anomalous pulmonary arteries:
10. 65

XXIII. Anomalies of great veins:
11. 61

13 12	1h	2 7 4	6 13	1 1	1 6 10 1	7 1 1	1 1	2 3	2 3 1	1 2 2	13	6 19
8 37	6d	16 6 2 1 3 2 2 1 3 1	1 1	8	2 3 8 3 6 2 3	6 2 3	1 1 1	5	2 1 6	1 5	8	—
37 16	15d	6w 18 4 22 32 12 7 6 5 3 5	2 4 17 29 3 6 16 18 3 6	2	2 4 17 29 3 6 16 18 3 6	2 4 17 29 3 6 16 18 3 6	2	7 17 4 9	8 7 3 2 2 3 1 2 2	13	6 43	
16 35	12d	9d 8 5 6 12 16 3 7 3 2 9	4 5 7 1 6 14 13 1 1 3	4	4 5 7 1 6 14 13 1 1 3	4 5 7 1 6 14 13 1 1 3	4	6 2 1 2 4 1 2 2 5	1 4 1 2 16	6 22	5	
4 24	9w	18 3 1 1 4 2 1	1 1 3	3 4 3	1 1 3	3 4 3	1 1 3	1 1 1 2 2 1	1 3 1	4 1 5	1	87
—	—	—	—	—	—	—	—	—	—	—	—	87
13	27 4 3	2 1 1	2 5 6	2 1 1	2 5 6	2 1 1	1 3	1 1 1	4 2	2 1 7	2 9	9
11 23	4	15 4 7 11	2 1 5	2 4 7 11	1 3 3 1 1 3 2 1	1 3 3 1 1 3 2 1	1 3	2 1 1 7	2 9	2 11	1 12	12
40 28	11d	9 21 16 5 1 39 8 17 12	24 2 2 11 7 15 3 1 5 6 6 4 3 5	4 1 3 26 4 20	15 12 9 6 2 3 1 2 21	15 12 9 6 2 3 1 2 21	4 1 3 26 4 20	2 12 7 1 6 7 40	8 48	48	48	48
24 24	11m	8 13 10 5 24 24 2 22 17	15 1 5 1 10 21 1 6 5 6 1 5 1 4 13 1 8	10 9 4 2 4 2 1 1 3 12 1	10 9 4 2 4 2 1 1 3 12 1	10 9 4 2 4 2 1 1 3 12 1	10 9 4 2 4 2 1 1 3 12 1	1 6 3 3 3 24	23 47	23 47	23 47	23 47
6 6m	6d	3m 3 5 5	2 3 3	1 1 2 4 3	6 1 1	6 1 1	1 1	1 1 1	2 3	6 2	6 2	2 8
7 13	10w	4 3 2 3	7 1 2 4 1 6 2	5 4 1 2 6 1 2	1 1 2 6 1 2	1 1 2 6 1 2	1 1 2 6 1 2	1 1 2	7 3	10	10	10
11 11	13d	2 5 2 7 11 11	6 7 9 1	1 7 8	2 2 2 2 1	2 2 2 2 1	1 1	2 4 4	1 4	5 16	11	16
—	—	—	—	—	—	—	—	—	—	—	—	110
8 38	9	19 5 2 1 1 1	2 3 4 2 2 1 5 1 2	1 3	1 3	1 3	1 1	5	4 3	1 8	2 10	10
6 13	4d	3 2 3 2 1 3	1 4	1 2 1 2 1 4	1 1	1 2 1 2 1 4	1 1	6 1	2	6 1 7	1 7	7
3 15 w	2d	6w 1 1 2 2 3	2	3 3 3 1	2 2	3 3 3 1	2 2	1 1	1 1	3 1 4	3 1 4	4
10 80	1d	32 7 2 1 1	1	2 3 2 3 1 2 2 2	2	3 2 3 1 2 2 2	2 1	2 1 1	2 1 10	2 12	12	12
13 68	5d	32 9 3 1 3	1	2 2 6 3 4 6 7 1 1 1	1 1 2	2 2 6 3 4 6 7 1 1 1	2 2 1	1 3 1 3 3	1 13	29 42	29 42	29 42
2 28	7m	14 2 3 9 9 1 2	1 2	1 2 1 2 1	1	1 2 1 2 1	1 1	1 1 1	1 1	1 3	3	3
10 2d	6w	7m 1 3 3 9 9 1 4	2	8 3 10 7 2	2	8 3 10 7 2	2 3 4 1	4 4 2	3 1 1 1	1 10	7 17	17
1 1d	2d	9 2 1 1 1 2	1	1 2	1 2 3 1	1 2 3 1	1 1	1 1	1 1	5 6	6 6	6
3 27	2d	9 2 1 1 1 2	1	1 2	1 2 3 1	1 2 3 1	1 1	1 1	1 1	3	—	—
8 71	5	37 3 4	1 1 1 2	2 4 1 4 2 4 2	2	4 1 4 2 4 2	1 1 2 1	2 1	2	8	8	8
4 44	7w	20 2 1 1 2 1	1	1 1 2 2 1 1	1	1 1 2 2 1 1	1 1 2 1	2 1	2	17 21	17 21	17 21
64 60	14d	20d 20 36 9 2 29	6 8	7 15 34 13 27 7 13 7 4 2 3	7 13 4 10 3	14 14 10 14 7 15 17 9 15	19 2 4 10 11 19 6	24 64	102 166	14 13	14 13	14 13
13 40	4d	3 7 6 1 4 1	1	3 1 1	1 1 1 1	3 1 1	1 1	1 1	2 13 1	6 6	6 6	6 6
—	—	—	—	—	—	—	—	—	—	—	—	—
6 5m	8h	4w 1 2 5 1 2 3 2	1 2 3 2 1	3 2 3 1	1 1 1 1	3 2 3 1	1 1 1 1	1 1 1	6	6	6	6
39 64	2d	3d 26 10 5 4 1 7 8	26 22 5 13 10 20 11 30 15 9 3	2 5 1 2 1 2	4 1 1 1 1 2	8 2 5 2 1 2 3 1 9 1 4	9 17	39 49 88	3 5 8	40 88	40 88	40 88
3 10m	Fetus	3d 1 1 3 1 3	2 1	1 1 1 1 1 2	1 1 1 1	1 1 1 1	2 1	1 4 2	2 44	46	46	46
2 21	17	2	2 2 2 2 2	1	1 1 2	1 1 2	2	1 2	2	2	2	2
3 87	45	64 3	1	1 1 3 1	1 1 3 1	1 1 3 1	1 1	3	3	3	3	3
9 25	Fetus	3 4 2 1	1 1 1 1 1 9 1	1 1 1 1 1 2	1 1 1 1 1 2	1 1 1 1 1 2	1 1	9 8	17	17	17	17
6 44	5	22 1 2 1 1 1	1 1 1 1 1 2	1 1 1 1 1 2	1 1 1 1 1 2	1 1 1 1 1 2	1 1	6 40 40	5 7 12	40 40	40 40	40 40
5 65	Fetus	3 1	1 3 2	5	5	5	1	1	10 4	10 4	14 14	14 14
10 65	Fetus	7d 1 2	1 1 1 1 1 1	1 1 1 1 1 1	1 1 1 1 1 1	1 1 1 1 1 1	1 1	2	1 11	18 29	18 29	18 29
11 61	3m	6 2 1	2 1 3 6 2	2 1 3 6 2	2 1 3 6 2	2 1 3 6 2	1 1	2	1 11	11	11	11

Abbreviations: A. = Aorta

The majority of cardiac defects are complicated, and it is often difficult, sometimes impossible, to say which is the primary lesion; many of the cases present other anomalies of equal importance with those with which they are grouped. A cross-index has therefore been made in the two columns next to the end, and the total relative frequency is to be found in the last column of the chart.

ANOMALIES OF THE PERICARDIUM.

Absence or Defect.—The Pericardium may be entirely *absent*, as in some forms of ectopia cordis, or its parietal layer may be more or less *defective*. Some forty-two cases are on record and the subject has recently been reviewed by Ebstein,¹ Plaut,² McGarry,³ and Cameron. The defect always involves the *left* side of the sac but it may vary from a localized hole with smooth edges lying over the pulmonary artery opposite the root of the left lung and communicating with the left pleura, to complete absence of the parietal layer, the heart lying in the anterior mediastinum, without any serous envelope. In all the cases recorded except the four above mentioned, the whole left and anterior walls of the pericardium are wanting, and the heart and left lung lie in a common cavity, the left pleura being continuous with the epicardium and the anterior and right walls of the sac being represented by one or more rudimentary folds; in the best developed cases two folds, one sagittal and one crescentic; spring from the diaphragm and are inserted, the one into the anterior mediastinum and the other posteriorly at or near the root of the left lung; in the more extreme cases the diaphragm is free and a serous fold encircles the base of the heart with the great trunks; in complete defects no trace of the parietal layer may exist, or it may be represented by a few fatty appendices arranged fringe-like about the base of the heart. The left phrenic nerve maintains its relationship to the pleuropericardial septum, running down parallel to the border of the sagittal rudimentary fold when this is present, and is displaced to the right in a degree increasing with the degree of the defect. This anomaly in the course of the nerve, and the serous investment of the margins of the defect, are points diagnostic of its congenital origin.

Pathogenesis.—An explanation of the condition is to be sought toward the end of the fifth week of fetal life, when the pericardial begins to be separated from the pleural cœlom. At this time the so-called pulmonary ridge, an elevation from the walls of the ducts of Cuvier, encircles, and gradually obliterates, the canal of communication between the two cavities, and descends to the septum transversum or primitive diaphragm as the pleuropericardial septum. Under normal conditions the left duct of Cuvier atrophies in early fetal life. Pericardial defect, with its invariable relation to the left pleural cavity, may well be due, as suggested by Perna, to a too early atrophy of this structure, dependent upon some anomaly of circulation in the great venous trunks, the arrested develop-

¹ *München. med. Wchnschr.*, 1910, lvii, 522.

² *Frankf. Zeitsch. f. Path.*, 1913, xii, 141.

³ *Anat. Record*, 1914, February 20.

⁴ *Trans. Chicago Path. Soc.*, 1914, ix, p. 148.

ment of the pulmonary ridge resulting leading to a localized defect (pleuro-pericardial foramen), or to the more or less complete absence of the pleuropericardial septum. In one of Keith's cases, a defect of the left pleuroperitoneal membrane is also to be concluded, for the heart, left lung, liver, spleen, and stomach lay in the left pleuropericardial cavity.

Clinical Aspects.—The defect in itself has no direct effect upon the heart, the patients reaching adult life, and sometimes even attaining advanced age without any untoward sign. Its *clinical significance* depends chiefly upon two factors: First of these is the abnormal juxtaposition of the heart and left lung, whereby the heart is exposed, without the protection of its serous envelope, to the many inflammatory changes prone to attack the pleura; some cause also, whether traction from adhesions with the constantly pulsating heart or friction with the surface of this, appears to act deleteriously upon the left lung and pleura, predisposing these to disease. Among the forty cases recorded the incidence of left-sided pulmonary complications is extremely large. Picchi's two patients died of left lobar pneumonia, Weisbach's of left purulent pleurisy, Powell's of left pneumothorax, Plaut's second case and Faber's of acute left-sided pleurisy and Baly's, Hughes', and Saxer's of pulmonary tuberculosis.

Secondly, the *cor mobile* resulting from the lack of pericardial attachment to the diaphragm and mediastinal structures, may lead to sudden kinking of the great vessels resulting not only in symptoms of precordial distress (Ebstein), but apparently, in one instance at least in death itself. In the case recorded by Boxall death occurred on the third day after confinement, apparently from the sudden slipping of the heart's apex out of a low-walled pouch formed by two rudimentary folds attached to the diaphragm, in the altered intrathoracic pressure following delivery. Thirty hours before death urgent dyspnoea, collapse, and a systolic murmur over the precordium suddenly appeared. Pulmonary thrombosis was suspected, but was not confirmed at autopsy, when the heart was found in the left pleura. The number of fatalities is high.

Diagnosis.—This is difficult, but does not seem impossible. The greatly increased mobility of the heart, its occasional hypertrophy either from this cause or from the traction of inflammatory fibrous tissue bands attaching it to the left pleura and diaphragm, and its frequent displacement to the left through such traction or from similar causes are the chief points. In spite of its rarity, pericardial defect should always be considered in the light of the x-ray findings.

In Faber's case, a man of fifty-one years, in good health until five weeks before death, when an extensive left pleural effusion developed, the heart was only moderately displaced to the right before aspiration, although the left chest was entirely dull; after the withdrawal of 2200 cc. of fluid the apex was evident in the third and fourth interspaces in the left anterior axillary line, and at a later aspiration of 3100 cc., the heart was felt in this region by the aspirating trocar. These facts supplied a basis for a correct diagnosis.

Unattached Pericardium.—Turner describes an adult male subject in whom the parietal pericardium was perfectly free from continuity

with the central tendon of the diaphragm or other structure, and was attached only about the base of the great vessels, closely embracing the heart, which could be drawn completely out of the chest (*cor mobile*), the inferior vena cava lay free in the thorax for an inch before piercing the pericardium. A similar condition was observed in the walrus and was thought here to be normal.

Diverticulum or Hernia Pericardii.—This consists in a localized bulging of the serous, or serous and fibrous, coats of the parietal layer, whereby a thin-walled cyst is formed, communicating with the pericardial cavity either directly by a narrow orifice, or by a tubular canal. An interesting example was seen by the writer in the Museum at Bologna, from a case published by Coen.¹ In this specimen a unilocular chamber of a capacity of 40 cc., formed by the protrusion of the serosa, projected from the right border of the parietal pericardium, as a kidney shaped tumor 17.5 cm. in circumference, and communicated with the interior of the pericardial sac by a minute orifice lying at the bottom of a small fossa. Coen gives an analysis of ten other cases in the literature.

This condition is of little clinical importance, usually remaining latent. Secondary pathological changes, such as calcification or fibrosis of the cyst walls, or occlusion of its orifice and consequent distension of its cavity may supervene, and make it an impediment to the heart's action. The possibility of a pericardial diverticulum should not be overlooked in the diagnosis of mediastinal tumors.

DISPLACEMENTS OF THE HEART.

Ectopia Cordis.—By this term is understood a displacement so that the heart passes out of the thorax, and comes to lie either upon the outer surface of the body or in the abdominal cavity. Full bibliographical studies, with reports of cases, are given by Jones,² and by Ellis.³ The latter, following Rauchfuss, recognizes three forms, (1) *cervical* heart, in which the organ lies high up in the neck; (2) *pectoral* heart with fissure of the sternum, and (3) *abdominal* heart in which the heart is projected through a defect in the diaphragm into the abdominal cavity.

The existence of cervical heart, or of pectoral heart with fissure of the upper part of the sternum and absence of pericardium, is not compatible with life; in abdominal heart on the other hand life is not necessarily shortened (witness Deschamps' case of a healthy soldier whose heart occupied the position of the left kidney in the lumbar region), and in pectoral heart with inferior sternal fissure and pericardium present, it might with due care be indefinitely prolonged. In Goode's⁴ patient, with fissure of the sternum below the manubrium, the heart was oiled every three hours and kept covered by a cardboard box, and the child did very well for a time. Ellis quotes a case in which a thin membrane covering the heart sloughed on the fifteenth day, and the outer skin

¹ *Bull. della Soc. Med. Chi. di Bologna*, 1885, xv, Fasc. 1.

² *Trans. Path. Soc.*, London, 1869, xx.

³ *Proc. Path. Soc.*, Philadelphia, 1906, p. 36.

⁴ *Virginia Med. Semi-Monthly*, 1904, p. 555.

covering the organ was successfully united by sutures. He suggests that such operative interference might be tried in suitable cases where the visceral pericardium is present.

Dextrocardia.—This term is applied clinically to all cases in which the heart is found displaced to the right side of the thorax. Pathologically two conditions must be distinguished. In the one the heart is simply displaced to the right as a result, usually, of acquired disease (*Dextro-versio cordis*). In the other the organ is also more or less altered in its position in the thorax, so that *the apex comes to point to the right*. In these latter cases two forms must again be recognized:

A. The heart is not transposed, but appears to have undergone a simple rotation from left to right on its vertical axis, so that its left chambers come to lie more anteriorly and its right chambers more posteriorly. The apex points to the right but is formed not of the left but of the right (venous) ventricle, which remains on the right side and receives blood from the right (venous) auricle into which the venæ cavæ empty. This, which is not a true transposition, is the condition present in the majority of the cases of congenital dextrocardia. It is well illustrated by Grunmach's¹ case (See Fig. 21.)

B. The heart may be completely reversed upon itself, those parts normally upon the left coming to lie on the right side, but the relation of the various structures to each other remaining unchanged, so that a complete mirror picture of the normal heart results. Here the apex, pointing to the right, is formed of what was normally the left ventricle, which now lies on the right side and communicates with the right (normally left) auricle which receives the pulmonary veins and is structurally the systemic auricle. In complete situs inversus this "mirror" condition is the rule, but true transposition of the heart only, without situs inversus is exceedingly rare, the only cases we know of on record being these of Graanboom² and Rokitansky.

The etiology of these two types of congenital dextrocardia differs widely. Nagel³ reviews six cases with clinical and autopsy reports in the literature, and demonstrates, with the aid of diagrams, that five of these, namely, those by Grunmach, Geipel, Löwenthal, Barmwerth and himself, belong to the type A above, in which the heart is not transposed, but presents simply a persistence of the embryonic stage, in which the apex was formed by the right half of the common ventricle. The fact that in all five of these cases the grave anomalies of pulmonary stenosis and ventricular septal defect were associated, affords convincing proof that a primary arrest of development had occurred.

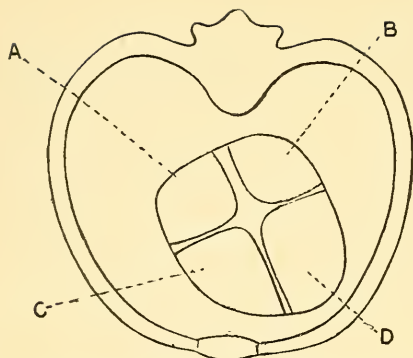
In the sixth case, on the other hand, that by Graanboom, in which there was true transposition of the heart, and the septum was entire, the probable explanation is to be sought, not in an arrest of development, but, with the causes of transposition in general, in the altered relation of the embryo to the primitive chorionic villi.

Congenital dextrocardia, unassociated with other anomaly, is not

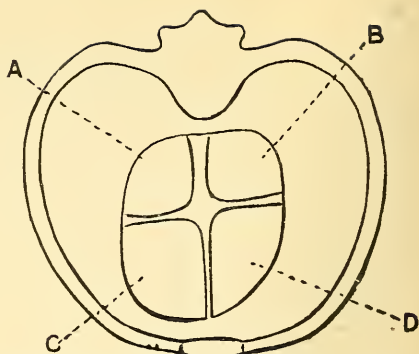
¹ *Berlin. klin. Wchnschr.*, 1890, No. 2.

² *Zeitschr. f. klin. Med.*, 1891, Bd. 18, 2.

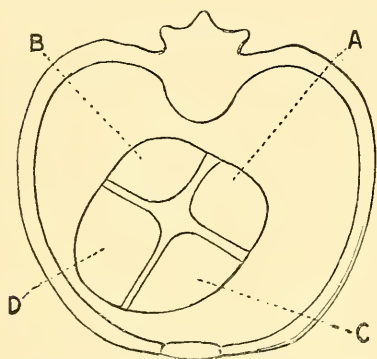
³ *Deut. Arch. f. klin. Med.*, vol. xevi, p. 552.



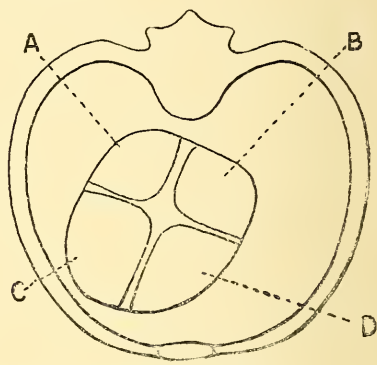
1. Normal heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



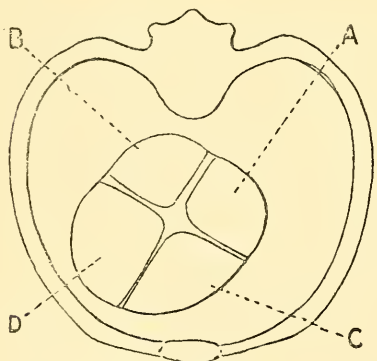
2. Embryonic heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



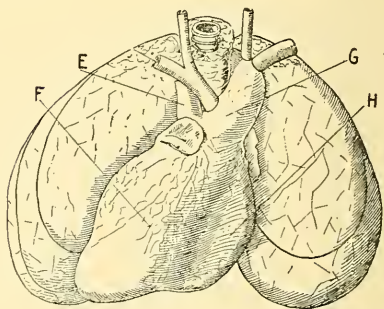
3. Mirror picture of normal heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



4. Pure congenital dextrocardia. A, caval auricle; B, pulmonary veins auricle; C, caval blood ventricle; D, pulmonary blood ventricle. Note similarity to No. 2.



5. Grunmach's case of congenital dextrocardia (mirror picture). A, caval auricle; B, pulmonary blood auricle; C, caval blood ventricle; D, pulmonary blood ventricle.

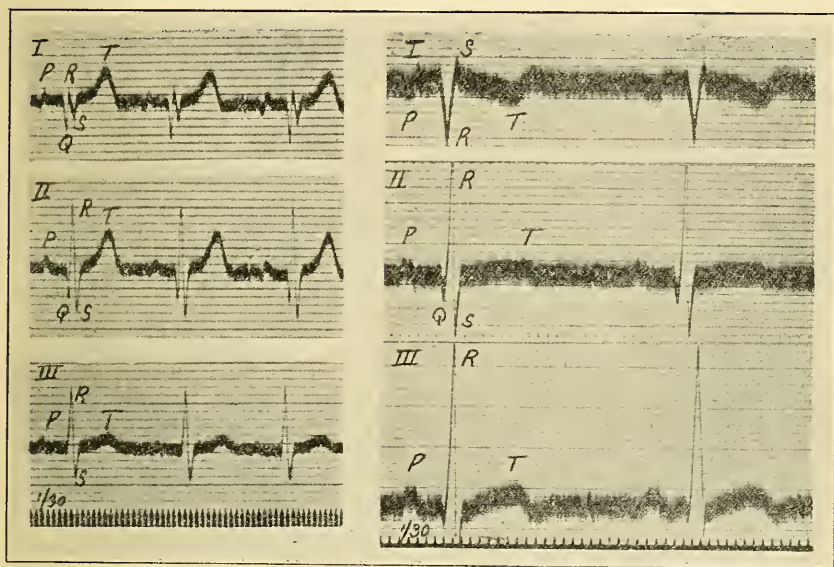


6. Grunmach's case of pure congenital dextrocardia (arrest in embryonic stage). E, vena cava superior; F, ventriculorum dextrum; G, aorta; H, ventriculorum sinistrum.

1, 2, 3, 4. Diagrams (1) showing normal heart; (2) embryonic heart; (3) mirror picture of normal heart; (4) heart in usual type of pure congenital dextrocardia; (5) from Grunmach's case of pure dextrocardia (mirror picture). Note that the apex is formed by the left (pulmonary blood) ventricle. (From Nagel's article on Pure Congenital Dextrocardia in the *Deutsches Archiv. f. klin. Med.*, xvi, p. 572.) (6) Grunmach's case of pure congenital dextrocardia; arrest of development, persistent embryonic stage. Note that the apex is formed by the right (caval blood) ventricle. (From his article in the *Ber. klin. Wchnschr.*, 1890, page 22.) The auricles are designated "caval" and "pulmonary," (according to the veins they receive), instead of right and left, in order to show the difference in situation in the mirror picture and in Grunmach's case, from that of the usual type of pure congenital dextrocardia (Grunmach's case).

itself of clinical significance and may be discovered accidentally with the heterotaxy that usually accompanies it, in a perfectly healthy subject, by physical and x-ray examination, which reveals the normal area of cardiac dulness on the right side, with corresponding location of sounds and fluoroscopic findings. Transposition of the heart, of the type usually associated with situs inversus viscerum (Graanboom's case) yields a characteristic electrocardiogram (Neuhof,¹ Lewis²), in that Lead I, shows a reversal of all curves, and Leads II and III, replace each other. This supplies a diagnostic point between the transposed and non-transposed forms of Congenital Dextrocardia and also distinguishes the former from a dextroversio, in which the electrocardiogram, although atypical, is not reversed. The curves in this latter condition have been studied by Neumann.³

FIG. 22



1. Electrocardiogram from a case of congenital dextrocardia with transposed (mirror-picture) heart. Note that: Lead I, is completely reversed in that P, R, and T, normally directed upward in this lead, here point downward. Lead II, has changed places with Lead III.

2. Electrocardiogram from a case of dextro-versio-cordis, i. e., simple displacement of the heart to the right. Here there is no reversal of leads, but Lead I especially deviates from the normal in Q and R. (From *Clinical Electrocardiography*, by Thomas Lewis, London, 1913.)

Incomplete Heterotaxy.—Of interest are three cases reported by Hickman, Royer and Wilson,⁴ and McCrae, of transposition of the viscera with only partial transposition of the heart, which maintained its normal position with *apex pointing to the left*, the ventricles and auriculo-ventricular ostia unchanged, but the auricles and great arterial trunks transposed, and the auricular septum defective. In McCrae's and

¹ *Jour. Amer. Med. Assn.*, 1913, lx, p. 1064.

² *Clinical Electrocardiography*, 1913, p. 100.

³ *Deutsch. med. Wchnschr.*, 1912, xxxviii, p. 1920.

⁴ *Arch. Pediat.*, 1908, xxv, 882.

Hickman's cases the pulmonary artery was atresic, in that by Royer and Wilson it was stenosed, and arose from the right ventricle with the aorta but in transposed relation. The ventricular septum was entire in McCrae's case, defective in the other two.

Intrinsic Displacement of Chambers.—Four interesting examples, in anencephaly and ectopia cordis, of displacement of the chambers upon each other, as a result of extraneous mechanical force exerted on the heart after it was fully formed, are reported by Jane Robertson.¹

ANOMALIES OF THE HEART AS A WHOLE.

Acardia, Hemicardia.—Where grave interference with the circulation occurs at a very early embryonic period, the heart may not develop at all (acardia), or it may be rudimentary (hemicardia). Such a condition usually develops in one member of a uniovular twin pregnancy in which anastomosis of the vessels of the two individuals can take place through their common placenta.

All degrees of acardia may occur and from the developmental standpoint the findings are extremely interesting. Thus Campbell and Shepherd report a case in which the circulation had been interfered with before the heart had formed at all, and in which the two dorsal arteries passing from the umbilical opening toward the head of the amorphous monster, represented a persistence of the early vitelline circulation. Kehrer² adds to an analysis of thirteen cases from the literature an account of a case of his own which is remarkable for the advanced state of the rudimentary organ. Cases not included in Kehrer's review are reported by Schubert³ and by Näcke and Benda.⁴

Multiple Hearts.—This phenomenon is commoner in animals. An explanation is perhaps to be sought in an irregular division of the omphalomesenteric or vitelline veins, from which the first heart *anlage* is derived.

Bifid Apex.—This may occur without other anomaly or complicating grave defects. The apex of the early embryonic heart during its amphibian stage, is bifid; a condition to be ascribed to the rapid downward growth of the apices of both ventricles at this time, so that a deep interventricular groove or cleft is formed. Obliteration of this cleft takes place in embryos over 11 mm. long, by the development downward of the embryonic apex, which occurs simultaneously with the closure of the interventricular foramen. In the adult mammalian heart bifid apex is thus to be ascribed to a persistence of the interventricular groove (Gegenbaur), due to an arrest of development of the embryonic apex, as is evidenced by the absence of the muscular vortex normally present here, each apex in the bifid state being formed independently from musculature derived respectively from the musculospiral and sinospiral bands (Mall).⁵ A deeply bifid apex is normal in the dugong; it occurs in 3 of Thérémín's 106 cases and in 15 of our series.

¹ *Jour. Path. and Bact.*, 1913, xviii, 211.

³ *Monatsch. f. Geburts.*, 1908, xxviii, 3.

⁵ *Anat. Rec.*, 1912, vi, 167.

² *Arch. f. Gynäk.*, 1908, lxxv, 121.

⁴ *Zentralbl. f. Gynäk.*, 1907, p. 17.

Diverticulum.—The heart may be prolonged into a hollow process. Arnold¹ reports a female child, aged two and a half months, a subject of congenital lues, in whom the apex of the left ventricle ran out into a hollow process which bent around like a hook, its blind end projecting upward and to the left. In Koller-Aeby's² case it formed a pulsating process with muscular walls descending from the apex of the left ventricle through a defect in the diaphragm to form part of an umbilical hernia. Diverticulum of the heart is rare and of no clinical significance.

Primary Congenital Hypertrophy.—Recently a number of observations have been published in which hypertrophy of the heart existed at birth. In 1898, Simmonds³ reported the first clear case of primary congenital hypertrophy. In a newly born child which died during a protracted labor all the organs including the kidney were normal, but the heart was greatly enlarged. It weighed 44 gm. (normal weight 19 to 20 gm.); the right ventricle was 0.75 to 1 cm., the left 1 to 1.25 cm. thick. The papillary muscles were small and took no part in the hypertrophy, thus indicating that this was not caused by overwork. Simmonds suggests that the hypertrophy may have been due either to some cause in early embryonic life, which may later pass away, or to Virchow's diffuse myomatous infiltration. Other typical cases of congenital hypertrophy without valvular disease, nephritis, or apparent cause, are reported by Effron,⁴ Kalb,⁵ and Ratner.⁶

Congenital Rhabdomyoma.—An interesting problem is presented by the occurrence in infants or young children of embryonic muscle tumors of the heart wall associated, in the majority of the cases, with sclerosis of the cerebral cortex. The condition was first described by von Recklinghausen and by Virchow and was first reported on this Continent by Knox and Schorer.⁷ Wohlbach⁸ has recently studied the 11 cases on record, and has added an observation of his own of an instance in which a rhabdomyoma of the wall of the right ventricle was associated with multiple nests of neuroglia in the spinal meninges. The child, a female, with hydrocephalus and spina bifida and paralysis of the lower half of the body from birth, died of scorbutus at ten months. The heart was very large, weighing 72.5 gm., with hypertrophied papillary muscles. Just below the pulmonary valve an ovoid nodule, 1.7 x 4 cm. wide, of grayish-red color and elastic consistence, lay imbedded in the interventricular septum and in the papillary muscle of the anterior tricuspid valve segment, to which it supplied chordæ. Microscopically it was composed of a delicate reticulum of connective tissue supporting heterogeneous cells having a more or less irregularly striated fibrillary matrix and containing in many instances large intracellular spaces and peripherally placed nuclei, the whole bearing a *bizarre* resemblance to the modified muscle cells (Purkinje fibres) of the adult heart.

An explanation of this remarkable combination of congenital cerebral

¹ *Virchows Arch.*, 1894, cxxxvii, 318.

² *München. med. Wchnschr.*, 1898.

³ *Munich Thesis*, 1906.

⁷ *Arch. Pediat.*, 1906. xxiii, 361.

² *Arch. f. Gynäk.*, 1907, lxxxii, 185.

⁴ *Zurich Thesis*, 1903.

⁶ *Berlin Thesis*, 1912.

⁸ *Jour. Med. Research.*, 1907, xvi, 495.

sclerosis with rhabdomyoma may be sought in the fetal malnutrition invariably present, which may have led to the vascular degeneration that must underlie such changes (Wohlbach).

ANOMALOUS SEPTA.

Anomalous cords, bands, or septa may arise within the heart, and lead, when sufficiently pronounced, to a division of the chambers, and the so-called double or supernumerary cavities.

Anomalous Septa in the Left Auricle (Double Left Auricle).—Of this interesting condition there are eight fully reported cases, by Church (1868), Fowler, Martin, Griffith (2 cases), Potter and Ransom, Borst, and Hosch,¹ all of which are summarized in an article by the latter writer. In these cases, a membranous diaphragm perforated by one or more openings stretches across the left auricle, dividing it into a right postero-superior chamber, which receives the pulmonary veins and contains the interauricular septum, and a left antero-inferior chamber, in which lies the auricular appendix and the mitral orifice. The blood from the pulmonary veins enters the large upper chamber and passes thence through the small opening in the diaphragm into the lower chamber to the mitral orifice. When the foramen ovale is patent, a large portion of the pulmonary blood may pass through the open foramen into the right auricle, thus depleting the greater circulation and throwing the bulk of the work on the right heart, which, as in this case, becomes greatly hypertrophied, and the left chambers very small.

Borst gives a careful anatomical study of his case, which throws much light on the etiology. In a woman, aged thirty-eight years, dying with failing compensation, the heart was of a quadrate shape, the right ventricle much hypertrophied and dilated, the left auricle also greatly dilated. There was no communication between the auricles, but the valvula formanis ovalis was absent. The left auricle was divided into a large upper cavity receiving the pulmonary veins and a small lower chamber containing the mitral orifice by a diaphragm which ran from above anteriorly and externally, downward, inward and backward. This diaphragm presented at its insertion below and behind, a round hole, 1 cm. across, which was the only communication between the two cavities through which the blood from the pulmonary veins could be transmitted to the mitral orifice.

Borst explained this anomalous diaphragm as the malposed *septum primum* which had been deflected to the left in the embryonic heart by a displacement of the pulmonary veins to the right, so that they entered the auricles between the *septum primum* and *secundum*, and had thus formed between them this large secondary cavity. The hole in this anomalous septum, which communicated with the smaller cavity below, he looks upon as the *ostium secundum* (patent foramen ovale).

Borst's explanation receives corroboration in a remarkable way from what may be termed a complementary case reported by Sternberg²

¹ *Frankf. Zeitsch. f. Path.*, 1907, i, 56.

² *Verh. der XVI Deut. path. Gesell.*, 1913, p. 256.

in which three auricular chambers were present, separated from each other by strong septa. The left chamber received the pulmonary veins and contained the mitral orifice, and communicated with the middle chamber by a large ovoid foramen (the ostium primum of Born), situated in the lower portion of the anomalous septum (S. primum) just above the mitral valve. This middle chamber received the superior cava only and communicated with the remainder of the right auricle, which received the inferior cava, by a large opening. Sternberg explained the formation of the middle chamber by a displacement to the *right* of the septum secundum, due to a malposition of the inferior cava, which entered too far to the *left*, and pushed the septum secundum to the *right*, just as in Borst's case the anomaly was due to the entrance of the pulmonary veins too far to the *right*, so that they cut off a middle chamber by pushing the septum primum to the *left*.

An *anomalous* band several cm. long and as thick as a knitting needle may traverse the left auricle. Cases were recorded by Browicz, Rolleston and Hosch.

Anomalous Septa in the Right Auricle.—These are quite different both in structure and origin from those in the left auricle. The condition was first described and figured by Chiari,¹ on the basis of 11 original cases. In all these a system of fine cords, or a reticulum of delicate tissue identical in structure with the Eustachian valve and attached to this or to the Thebesian valve stretched across the auricle to be attached to the crista terminalis or auricular septum or other points. Similar structures in the right auricle have been recorded, and are to be ascribed, as Chiari pointed out, to a persistence and anomalous development of the *septum spurium* or of the right and left valvulæ venosæ. These are the lips of the opening of the embryonic sinus venosus into the right auricle. In normal development they become merged with the Eustachian and Thebesian valves, and with the septum secundum. In a case by Lesieur and Froment² of a gaping foramen ovale with an anomalous valve of Thebesius, 6 cm. high, which projected as a fenestrated, incompletely attached, shelf across the right auricle, these authors ascribe both anomalies to the maldevelopment of the *valvula venosa sinistra*, which failed to close in the foramen ovale by merging with the septum secundum. A connection between these two anomalies is further established in Ebbinghaus's case, in which Chiari's fenestrated network extended across the auricle from the Eustachian valve, and the interauricular septum showed fifteen small and two large perforations. Persistent left superior cava is also frequently associated.

Clinical Aspects. When uncomplicated by other defects, such septa may exist without giving any evidence of their presence. All the cases of double left auricle recorded were in adults, except that by Hosch. There are certain dangers, however. When the septum is strongly developed, it is liable to hamper the blood stream. Church's case, and Borst's, both died at thirty-nine years of failing compensation, and Borst's patient suffered from earliest youth from dyspnœa. Again the fine

¹ *Ziegler's Beitr.*, 1897, xxii., 1.

² *Lyon Médical*, 1911, xcvi, 1045.

reticulum that occurs in the right auricle may supply a possible nidus for thrombotic processes, which may lead to pulmonary embolism and death. This happened in Chiari's first case, and thrombosis is related also by Thilo and Thorel.

Anomalous Septa in the Ventricles.—These again have a very different origin from those in the auricles. The commonest form is a septum shutting off the conus from the sinus of the right ventricle, which probably represents arrest at an early stage in the development of the heart, explained by Keith as a "persistence of the lower bulbar orifice." Such septa have usually undergone much fibrous thickening, and have been ascribed by many observers to inflammatory contraction, but in a case reported by Bohm all evidence of fibrosis was absent, and the conus was separated from the sinus by a simple muscular ridge. Two cases reported by Stephen Mackenzie¹ of hearts showing "three ventricles," separated by incomplete septa, probably belong here.

In another type of anomalous septum, a rudimentary chamber giving off the pulmonary artery, or the (transposed) aorta is cut off from a common ventricle which receives both auriculoventricular orifices, by what appears to be the malposed and defective interventricular septum. This type is well illustrated by the Holmes specimen in the McGill Museum (described and figured under Triloculate Heart, page 373). There are eight similar cases in the literature, but in all except that of Holmes the aorta and pulmonary artery were transposed.

Anomalous chordæ tendineæ frequently cross the ventricles at irregular points. They may consist of fibrous tissue with or without ordinary heart muscle fibres, or they may contain fibres from the auriculoventricular bundle. These fibres have been studied by Tawara,² who gives a review of the literature, and by Mönckeberg.³ They are explained by the latter, as an irregular differentiation of the spongy musculature of the embryonic ventricle, which may or may not contain Purkinje fibres according to their distribution. Such abnormal chordæ may cause loud musical murmurs. A case in point is related by Hamilton.⁴ The patient was a man of forty with symptoms of aortic insufficiency, who presented, in addition to a soft diastolic murmur with the localization characteristic of this lesion, a second murmur, also diastolic, but musical in character, which had its maximum intensity at the third left interspace, but was widely propagated over the chest, and was so loud as to be audible two feet away from the patient. The autopsy, performed by Adami, showed this musical murmur to have been produced by an anomalous cord which sprang from a small papillary muscle of its own, and crossed the auricular surface of the aortic cusp. The aortic valves were thickened and incompetent.

Anomalous chordæ passing from the aortic cusps to the base of the aorta (Rohrle), and from pulmonary cusp to base of pulmonary artery

¹ *Trans. Path. Soc. Lond.*, 1880, xxxi, 63.

² *Ziegler's Beitr.*, 1906, xxxix, 563.

³ *Verhand. XII Deut. Path. Gesell.*, 1908, p. 160.

⁴ *Montreal Med. Jour.*, 1899, xxviii, 508.

(Poscharissky) and from left auricle to left ventricle through the mitral orifice, have been recorded.

FIG. 23



Aberrant chordæ tendinæ in left ventricle producing a loud musical diastolic murmur. (From a specimen in the McGill Medical Museum, presented by W. F. Hamilton and J. G. Adami.)

DEFECTS OF THE INTERAURICULAR SEPTUM.

These may consist of a simple patency of the foramen ovale, or true defects of the interauricular septum, situated above or below the foramen, and single or multiple, may occur. In this series, the foramen ovale was patent 192 times, and there were 46 true interauricular defects, of which 15 were in its upper and 18 in its lower part, and 13 were multiple. In 14 cases the septum was rudimentary and in 5 it was absent (cor biventriolare).

Patent Foramen Ovale.—This orifice, which in the fetus is widely open, allowing of the passage into the systemic circulation of aerated placental blood, usually closes after birth, but its persistence in adult life as a valvular slit is so common that this can scarcely be considered abnormal. Among 711 adults, Zahn found the foramen open in 139, and in Adami's records of 1374 autopsies at the Royal Victoria Hospital, Montreal, it occurred 199 times (14.5 per cent.). From the combined statistics of Bizot, Ogle, Klob, Wallman, Rostan and Hinze, we learn that among 2087 hearts examined, the foramen was patent 632 times (30 per cent.) (Herxheimer).

A widely patent foramen is, however, a true anomaly, which, by allowing free communication between the auricles, may give rise to various disturbances. Of the 191 cases in this series, 89 were of this type, and of these, 18 were instances of pure patency, unassociated with other defect, and were therefore classed as the primary lesion, as affording material for the study of special symptoms and signs. In some cases the opening is very large, the size of a "two-shilling piece" (Peacock), in others it is a "circular opening with thickened edges admitting a penhandle," and in others again, it is valvular in form but an elliptical gap remains between the concave free margins of the annulus ovalis and the valvula foraminis ovalis, which are here incomplete.

The causes of patency may lie in a rise of pressure in the right chamber after birth, preventing the firm apposition of the valvula foraminis ovalis from the side of the left auricle, and its subsequent closure; this is the case in the majority of the cases complicating other defects, such as pulmonary stenosis. Or the foramen may remain open as a result of a true arrest of growth of the primitive septa, especially of the septum secundum, an event which may be shown in the specimen by an incomplete development, absence, or fenestration of the annulus ovalis. The association of an anomalous network springing from the Thebesian or Eustachian valve, with a patent foramen or perforated valvula foraminis ovalis, and the dependence of both anomalies on the persistence of the embryonic sinus-valvular apparatus, has been mentioned. Persistence of the left superior vena cava belongs to the same complex, as is illustrated by its occurrence in the case of Berthel.

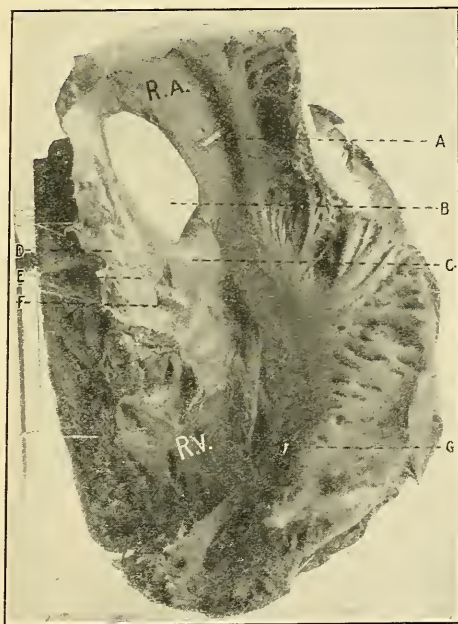
Such a combination is well illustrated in a remarkable case in the McGill Museum from the service of C. F. Martin. The patient was a woman of thirty-eight, presenting the symptoms of mitral stenosis with auricular fibrillation, and a greatly dilated heart. At the autopsy the mitral valve was markedly stenosed and the foramen was widely patent, a permanent elliptical opening 2.5 x 1.5 cm. large, with calcified lower border existing. The auricular septum behind this was greatly thinned and dilated and was bordered in the right auricle by a flattened and much fenestrated ring representing the defective annulus ovalis, and the Thebesian valve was enlarged and retiform. On the side of the left auricle at the right posterior margin of the septum, there was a curious valvular-looking pocket 2 cm. deep, the free margins of which were attached to the auricular wall by a plexus of tendinous cords. At the foot of this pocket a channel could be traced by a fine probe which communicated with the right auricle above the Eustachian valve. The coronary sinus and veins were hugely dilated.

Defects in the Upper and Posterior Part of the Interauricular Septum.—These are extremely rare. Two types may be distinguished, one in which the defect is associated with an anomalous disposition of the great veins, which is probably the primary condition, and another in which no such associated anomaly has been demonstrated, and which on closer investigation may be found to belong in the same category with the first, or which may require a different explanation. A series of cases has been recorded, in which a large defect occupies the upper margin

of the auricular septum, directly under the orifice of the superior vena cava, which is displaced somewhat to the right, so that its orifice looks into both auricles through the defect. A displacement to the right of the pulmonary veins, so that these enter either the superior vena cava just before this vessel reaches the heart, or the right auricle itself, has been noted and is to be considered the primary anomaly. Paltauf thought that the hole in the septum was not a defect at all, but represented the orifice of the right pulmonary vein, which entered here directly above the septum, with the superior cava. In Hepburn's case the wall of the auricles was directly continuous with the wall of these two veins, which here entered the auricle together. The foramen ovale was patent in some cases, and is mentioned as closed in others.

Rokitansky described 7 cases of a similar anomaly, in which the *inferior cava* looked into both auricles through the defect. In one of these the right pulmonary veins entered the right auricle.

FIG. 24



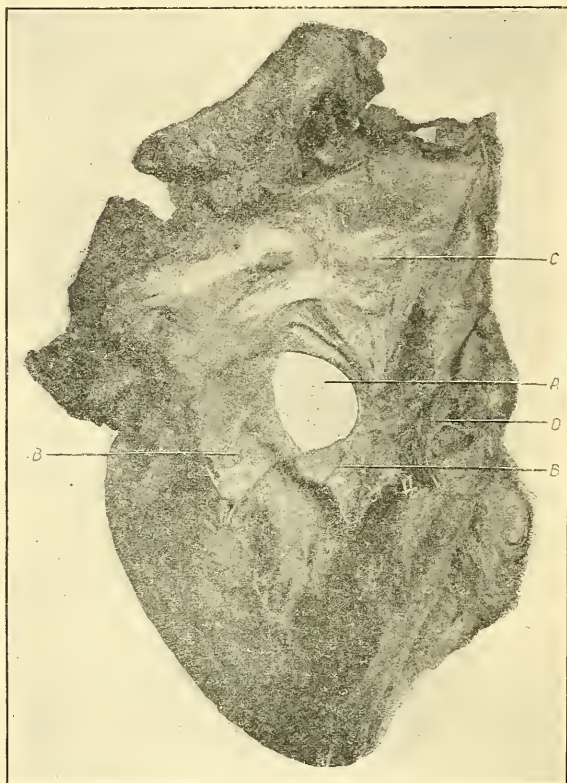
Defect in the upper part of interauricular septum (persistent ostium secundum), with pulmonary dilatation, sclerosing pulmonary endocarditis with calcification, and hypoplasia of the aorta. From a woman, aged sixty-four years. Right chambers laid open to show: *A*, hypertrophied and dilated right auricle; *B*, large defect in the upper part of interauricular septum bounded below by *C*, a stout muscular partition, the defective auricular septum; *D*, absence of annulus ovalis and of Eustachian valve; *E*, dilated coronary sinus guarded by a defective valve of Thebesius; *F*, entrance of superior vena cava; *G*, entrance of inferior vena cava. (From a specimen in the Medical Museum of McGill University, Montreal. Presented by F. W. C. Mohr. Reported by M. E. Abbott and J. Kaufmann.)

In a specimen in the McGill Museum, reported by Abbott and Kaufmann¹ (see Fig. 24), a large ovoid defect 3 x 3.5 cm. in diameter occupies

¹ *Jour. Path. and Bacteriol.*, 1910, xiv, 525.

the upper and back part of the septum, but the superior cava is not displaced, but enters the right auricle in its normal situation and is separated from the defect by a strong muscular cushion. The position of the right pulmonary veins could not be ascertained, but the annulus ovalis and Eustachian valve are absent, and it is probable that we are here dealing with an entirely different condition, namely, a huge persistent ostium secundum (patent foramen ovale) which has escaped closure

FIG. 25



Heart showing (A) defect of interauricular septum below (persistent ostium primum), with (B) cleavage of right anterior segment of mitral valve. (C) Interauricular septum above showing closed foramen ovale. (D) Left posterior mitral segment. From a woman, aged thirty-two years, without cardiac symptoms, dying of perforative appendicitis. (From a specimen in the Pathological Museum, McGill University.)

through lack of development of the secondary septum. The heart was from a woman of sixty-four in good health until the last six years of life, when cyanosis began to manifest itself. The case terminated with failing compensation and profound cyanosis, and is further remarkable in that extensive endarteritic changes with extreme calcification had taken place in the pulmonary valves, as the result of the excess of work done by the pulmonary circulation.

Defects in the Lower Part of the Interauricular Septum.—These are somewhat more frequent than are defects at the upper part of the septum, but are also rare. They are explained as a persistence of the *ostium primum*, the septum primum having failed to descend and unite with the cushion between the auriculoventricular orifice. Such a defect has a very characteristic appearance. It lies directly above the ventricles, may be of very large size, and is of a crescentic or semilunar shape, the thin border of the auricular septum, which forms its upper boundary, arching across the venous ostia to join the lower margin formed by the bases of the mitral and tricuspid valves, which are commonly deformed.

A common and interesting associated anomaly is a division of the anterior segment of the mitral valve, which is cleft from its free border up to its insertion, the two parts converging here to an acute angle, being widely separated below. In five of the seven cases of this defect reported by Rokitansky this cleavage occurred. It is well seen in Fig. 25, from a specimen in the McGill Museum. Here the foramen ovale was closed, as in the cases reported by Griffith,¹ Soldner,² Moore,³ and Peacock.⁴ It was patent in the cases by Reineboth,⁵ Thomson,⁶ Kilduffe,⁷ and Sternberg.⁸

Multiple Defects.—The valvula foraminis ovalis is not infrequently perforated by numerous small openings, as in a specimen (Fig. 26) in the McGill Museum, and in several cases in this series. This recalls the fenestrated septum seen in birds, and suggests an arrest of development at this stage. In a case reported by Dublitzhaja, of combined defects of the auricular and ventricular septa, the auricular septum, defective below, "hung like a curtain over the common ventricle," there was a large patent foramen ovale, and also a large hole at the upper and posterior border of the valvula foraminis ovalis. An almost identical case is reported by Ebbinghaus. In a man of fifty-two, there were fifteen small perforations and two large holes at either border, representing the persistent ostium primum and secundum (patent foramen ovale), and the right auricle contained an anomalous network.

Aneurismal Pouching.—Aneurismal pouching of the fossa ovalis is sometimes seen (Figs. 26 and 27). In most cases the convexity of the pouch is toward the left auricle, indicating a rise of pressure in the right heart before death.

Secondary Pathological Changes.—The alterations in the circulation produced by large defects in the interauricular septum induce various secondary results. Hypoplasia of the aorta and a corresponding dilatation of the pulmonary artery are common, and the latter vessel may also be atheromatous from excessive strain. Hypertrophy and dilatation of the heart are the rule, and this may be confined to the right chambers

¹ *Manch. Med. Chron.*, 1902, iv, 383.

² *Munich Thesis*, 1904.

³ *Trans. Path. Soc.*, London, 1881, xxxii, 37.

⁴ *Ibid.*, 1847, i, 61.

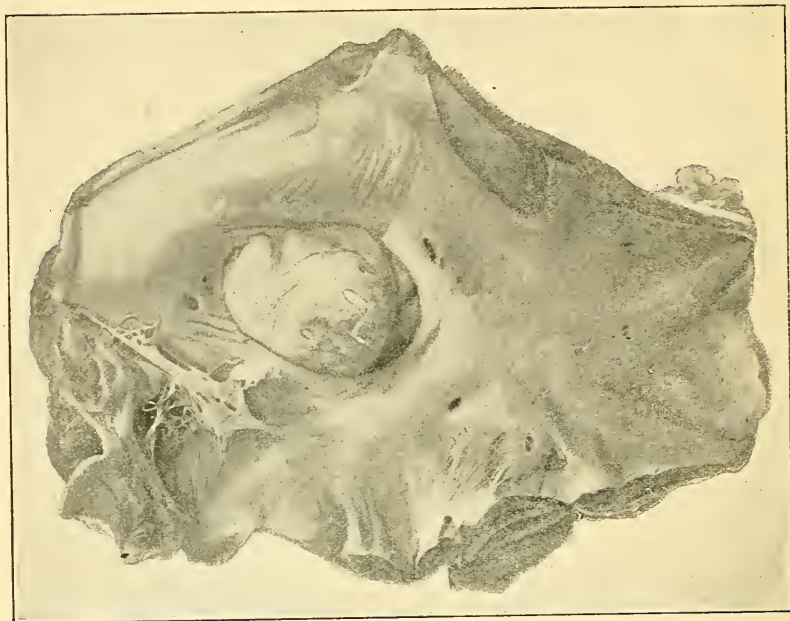
⁵ *Deut. med. Woch.*, 1895, xxi, 870.

⁶ *Proc. Anat. Soc.*, 1902-3, xxxvi.

⁷ *Am. Jour. Med. Sc.*, 1914, cxlvii, 880.

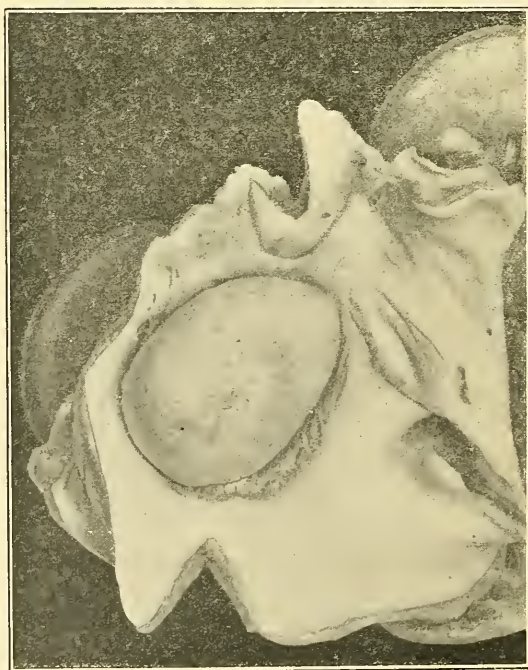
⁸ *XVI Verh. d. Deut. Gesell.*, 1913, p. 253

FIG. 26



Fenestrated membrane bulging into fossa ovalis. (From a specimen in the Pathological Museum, McGill University.)

FIG. 27



Bulging of fossa ovalis into left auricle. Valvular patent foramen ovale. (From a specimen in the McGill Pathological Museum.)

or may be generalized, the changes in the right side almost always preponderating. In none of the cases in this series was the left ventricle hypertrophied in excess of the right. Both auricles are usually much dilated and in four of our cases this took place without any increase in size of the ventricles. Congestive changes and œdema of the lungs, enlargement of the liver, and passive congestion of all organs usually occur as late results of the overloading of the pulmonary circulation.

Symptoms and Signs.—Large defects in the interauricular septum may exist without giving any sign or symptom of their presence and without interfering with the duration of life of the individual. The characteristic feature of the majority of the cases may be summed up as an absence or but very slight manifestation of cyanosis, in the presence of distinctive physical signs of the defect. In a few rare instances, symptoms of congenital cyanosis have set in, in cases of uncomplicated foramen ovale in very early life. There are three such in our series, one by Johnson, of a man aged twenty-seven with moderate cyanosis and slight clubbing, and the others by Simmons¹ and Foster² in infants, showing cyanosis and dyspnoic attacks.

The above statement is especially true of defects at the *upper part* of the septum. All the patients in this series reached middle life without giving any evidence of disease, and with the exception of two cases, all died of independent conditions unassociated with the defect. In Greenfield's case, a man, aged fifty-three years, failing compensation set in eighteen months before death and cyanosis was marked at the close.

Not infrequently symptoms first develop after some event, such as an intercurrent pneumonia, has embarrassed the pulmonary circulation, and thus caused a rise of pressure in the right auricle, followed by a passage of venous blood from right to left through the defect. The picture is usually that of a relative mitral insufficiency, with marked cyanosis supervening as a terminal event. These are the cases of *la cyanose tardive* described by Bard and Curtillet as characteristic of auricular septal defects. The hypoplasia of the aorta so often associated with patent foramen probably assists in the development of failing compensation, and therefore forms an essential part of the picture.

Auricular septal defects are not infrequently associated with mitral stenosis. Such cases, of which there are seven in our series, usually run their course under the guise of the complicating mitral condition, the defect probably adding a factor in the development of the cardiac distress. An example of the absence of characteristic symptoms in extensive communication between the auricles is seen in Dr. Martin's case of mitral stenosis with open foramen. The clinical picture here was that of the terminal stages of uncomplicated mitral stenosis, and the degree of cyanosis was not greater than might have been expected in such a condition. A presystolic thrill with maximum intensity at the left fourth interspace, and a presystolic murmur audible towards the base which disappeared as the end approached, were the only evidence of the defect.

¹ *Inter. Med. Jour. Austr.*, Feb. 20, 1906.

² *Dublin Quarterly Jour. Med.*, 1863, xxxvi, 112.

Pallor of the surface is a common characteristic (Mouls¹) as is also a certain delicacy of build, the result evidently of the diminished amount of blood in the systemic circulation. Dyspnoea and tachycardia, bronchitis and signs of congestive changes in the lungs and of passive congestion in the viscera and enlargement of the liver are also common, from excess of blood entering the right heart. When, in adults with these symptoms, and with cyanosis slight, absent, or of extremely late appearance, we find distinctive physical signs of a defect localized over the upper and middle thirds of the heart, we may feel fairly sure that we are dealing with an auricular septal defect. A correct diagnosis was made on this basis in a patient at the Royal Victoria Hospital whose heart is in the McGill Museum. In a woman of twenty-eight years, of somewhat infantile appearance, in whom cyanosis was entirely absent, a loud harsh systolic murmur with maximum intensity at the third left interspace, 4.5 cm. from the midsternum, was heard loudly all over the front of the chest and over the left back, the cardiac dulness was greatly increased in all directions, and there was a marked systolic thrill at the base to the left of the midsternum, extending downward to the top of the fourth rib. The neck veins were much distended, but no positive venous pulse was detected. Death occurred from chronic interstitial nephritis. The autopsy showed a large patent foramen ovale admitting the thumb, with cribriform perforation of the valvula foraminis ovalis, hypoplasia and slight coarctation of the aorta, and infantile genitalia.

The slight degree of cyanosis that characterizes these cases and the effect of the lesion upon the duration of life are well shown by the analysis of the 43 cases of auricular septal defects classified as the primary lesion in this series. Cyanosis was *entirely absent* in 21 cases. In 2 of these death apparently due to the defect occurred in 4, in 2 cases from failing compensation, in 1 from sudden collapse, and in 1 (Popper²) by sudden development of œdema and dyspnoea. *Terminal cyanosis* occurred in 13 cases of the series. The ages of the patients ranged from ten to sixty-four years, and death occurred from pneumonia in 2, from failing compensation in 6, and from cerebral hemorrhage in 1 (Ebbinghaus). In 4 other cases of the 43, cyanosis was described as *slight* and in 3 only as *moderate* (Johnson, Foster, Simmons).

Physical signs are sometimes absent, but, in widely patent foramen ovale, and in defects at the lower part of the septum, a sufficiently characteristic murmur is usually present, and sometimes a corresponding precordial thrill. In defects at the lower part of the septum in which extensive deformities of the auriculoventricular cusps are usually associated, the murmur produced is often heard best at the apex, and is "confused," or "roaring" in character. It was associated in 4 out of 10 cases analyzed with a thrill continuous or systolic or "presystolic" in rhythm. In widely *patent foramen*, the murmur is usually systolic or presystolic and is sometimes soft, but often harsh and rasping, or of a peculiar blowing, or even musical character, and may be localized in the second,

¹ *Rev. Mens. des Mal. des Enfant*, 1888, vi, p. 151.

² *Wien. klin. Woch.*, 1909, No. 16, p. 562.

third or fourth interspace near the left sternal border, or over the mid-sternum in this situation, or may be diffusely heard over the precordium. It is *frequently audible in the left back*, and may be transmitted to the apex and axilla, or (occasionally) to the left subclavicular region (Markham's¹ case), or may be heard loudly over the whole chest. Among the 18 cases of patent foramen analyzed, a murmur of the above character was noted in 14. In 9 it was systolic, in 3 presystolic, in 2 it varied from presystolic to systolic, and in 1 only (Bard and Curtillet) it was diastolic in rhythm. In 3 of these cases the murmur was associated with a thrill of corresponding localization and rhythm.

Both murmur and thrill may vary in intensity and in rhythm with the position of the patient being noted as presystolic or systolic on different examinations. This inconstancy may be a useful diagnostic point (Ohm).

When an organic mitral insufficiency is combined with a patent foramen, the regurgitation of blood through the defect into the right auricle during systole of the ventricles may give rise to a *positive venous pulse* in the neck, without the presence of tricuspid insufficiency. Cases are reported, confirmed by autopsy, in which the tricuspid was healthy, and in which no signs of tricuspid regurgitation existed during life. When mitral stenosis is present this sign is of no value, as it is likely to be due to the auricular fibrillation so frequent in this condition.

Paradoxical Embolism.—A serious clinical significance is given to patent foramen ovale by the fact that particles may be carried through the defect from the venous circulation to the arteries of the brain, or from the systemic arteries to the lung, leading to instant death. This possibility was first pointed out by Cohnheim in an observation of a woman dying of embolism of the middle cerebral artery. The foramen admitted three fingers, the arterial system was clear, while the primary thrombi lay in the veins of the lower extremities. Ohm² collected 11 such cases from the literature in which an embolus from a thrombosed vessel or a metastasis from a new growth undoubtedly passed through the open foramen and added an original case. Ballet³ collected 6 cases of death from cerebral abscess from infected emboli in which both cardiac and cerebral symptoms were present during life. In 3 of these there was a patent foramen, in 2 a defect of the interventricular septum. Verse⁴ described 2 typical cases.

DEFECTS OF THE INTERVENTRICULAR SEPTUM.

The interventricular septum may be completely absent (cor biatriatum triloculare), or it may be rudimentary, represented by a falciform process growing up from the lower and anterior wall of the ventricle, or localized defects may occur. These usually lie at its base, and are relatively common in association with other anomalies, but are not frequent alone. Defects elsewhere than at the base, whether alone or in combination, are among the rarest of cardiac anomalies.

¹ *Trans. Path. Soc.*, London, 1881, viii, 142.

² *Zeit. f. klin. Med.*, 1907, lxii, 374.

⁴ *XIII Verh. Deut. Path. Gesell.*, 1909, p. 215.

³ *Archiv. gén. de méd.*, 1880.

Defects at the Base.—The cases of congenital cardiac disease here studied have been drawn only from reliable sources, and all have post-mortem reports attached, which should make them a fair index of relative frequency. It is therefore of interest to note that among them, while defects elsewhere in the septum are exceedingly rare, “pure” defects at the base are commoner than is usually supposed, and, in combination with other defects they rank as the most frequent cardiac anomaly.

Among the 631 cases, a defect at the base occurred 177 times, elsewhere than at the base, 12 times, making 189 cases, or 30 per cent. Of the 177 defects at the base, 34 were classed as the primary defect and 143 complicated other conditions. Of the 34 “primary” defects at the base, 8 were combined with *rechtslage* of the aorta, and in 1 of these there was also pulmonary hypoplasia; in another there was pulmonary hypoplasia without *rechtslage*; in 3 there was a patent ductus arteriosus, leaving 22 “pure” defects at the base unassociated with *rechtslage* or other anomaly except (in 5 cases) bicuspid or defective aortic or pulmonary valves.

Of the 143 defects at the base complicating other anomalies, 75 were in cases of pulmonary stenosis or atresia, in 53 of which there was also *rechtslage* of the aorta. Of the remainder, 26 were in transposition of the great trunks, 3 in other defects complicated by *rechtslage*, and 13 in persistent truncus arteriosus. That is to say, in 42 other cases the defect was associated with an irregularity of development of the great trunks. In the remaining 26 of these 143 cases, the septal defect was associated with tricuspid atresia in 9 cases, with mitral atresia in 1, with aortic stenosis or dextrocardia in 2, and with partial defect of the aortic septum in two.

Pathogenesis.—The combination of a defect of the interventricular septum with pulmonary stenosis and *rechtslage* of the aorta constitutes one of the commonest forms of congenital cardiac disease. So frequent is the combination that a causal connection between the three conditions has been sought, and rival theories as to which is the primary lesion have been suggested.

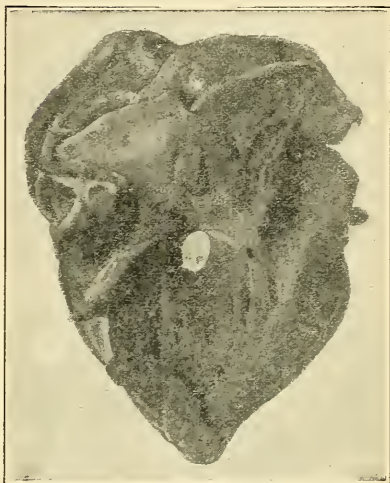
Much light was thrown upon this subject by Rokitansky, who concluded that non-inflammatory pulmonary stenosis, displacement to the right of the aorta, transposition of the great arterial trunks, and defects at the base of the interventricular septum were alike dependent upon a common cause, a deviation of the aortic, so that it failed to unite with the interventricular septum. He divided the latter into a part anterior, and one posterior to the undefended space, and classified defects at the base according as they lay in the anterior part of the anterior septum, in the posterior part of the anterior septum, or in the posterior septum. He pointed out that their usual situation was in the “posterior part of the anterior septum,” that is, just anterior to the pars membranacea, in which case he believed they were practically invariably associated with a malposition of the arterial trunks. Keith has suggested that in the large number of cases in which a septal defect is associated with stenosis of the conus of the right ventricle the defect is a direct

result of the inadequate expansion of the bulbus cordis to form the infundibulum of the right ventricle.

Later advances in embryological knowledge show that the aortic septum is prolonged downward to assist in closing the interventricular septum at the undefended space, instead of the interventricular septum growing upward to form part of the aortic wall, as Rokitansky supposed. Moreover, independent defects of the interventricular septum in this situation, unassociated with any alterations in the relations of the great arterial trunks, and evidently not of inflammatory origin, may and do occur. This is so in the specimen seen in Fig. 28, and in cases reported by Orth,¹ Arnold, Preisz,² and Hart.³ Such conditions cannot be explained on Rokitansky's theory as due to deviation of the septum, or, a deficient expansion of the infundibulum, but are due, as Keith himself points out, to a primary arrest of growth of unknown origin. In Hart's case an interesting associated anomaly, which may have had some bearing on the defect, was an anomalous cord which extended from the lower border of the conus of the right ventricle through the septal opening, to the anterior segment of the mitral valve.

Pathology.—The commonest situation for the defect is directly beneath the aortic cusps and just anterior to the undefended space (Rokitansky's posterior part of the anterior septum) (Fig. 28). Here it lies with the fleshy muscular septum before it and the thin pars membranacea behind, and opens in the right heart beneath the septal cusp of the tricuspid, sometimes perforating this or bulging the (adherent) tricuspid leaflet before it, or opening into the right auricle directly above the base of the tricuspid, thus establishing a communication between this cavity and the two ventricles. More rarely the defect is placed farther forward in the septum in its anterior fleshy part, just behind the front wall of the heart, and is separated behind from the undefended space by a muscular column, opening into the conus of the right ventricle below the pulmonary valves. (Rokitansky's anterior part of the anterior septum). Examples are the cases by Coupland⁴ and Rolleston.⁵ Keith points out that in these cases, the defect is evidently in the musculature of the interbulbar septum, *i. e.*, it is in that part of the interventricular septum

FIG. 28



Defect of the interventricular septum at undefended space. Heart of infant. No other anomaly. (From a specimen in the McGill Pathological Museum.)

¹ *Virchows Archiv*, 1880, Bd. 82, 529.

² *Virchows Archiv*, 1905, Bd. 181, p. 73.

³ *Trans. Path. Soc. London*, 1879, xxx, 226.

⁴ *Ibid.*, 1891, xlii, 65.

⁵ *Ziegler's Beiträge*, 1890, Bd. 7, 245.

which in the embryo formed the proximal part of the bulbus cordis before its division into the conus of the pulmonary artery and the vestibule of the aorta.

The defect varies in form and size from a pinhead perforation with tendinous edges, a round or oval hole admitting a goose-quill, knitting needle, index finger, etc., to a large triangular, semilunar, or crescentic space with thick-walled lower muscular border. Aneurismal pouching of the pars membranacea into the right ventricle may occur, with multiple sacculations perforated at their apices at one or more points (*vide infra*).

Quite frequently the margins of the defect with the adjacent valves are the seat of an acute inflammatory process which apparently originates at this point, because, as the seat of greatest strain, it affords a site of lowered resistance. Such a case is reported by Gordon.¹ In a boy aged five years who died of malignant endocarditis, a marked precordial thrill, and loud, harsh systolic murmur over the whole chest, with maximum intensity at the third and fourth left cartilages, indicated the septal defect. The autopsy showed a congenital opening, admitting a lead pencil, between the ventricles. The pulmonary valves and adjacent wall of the right ventricle were the seat of a number of large grayish-green vegetations which extended below the level of the interventricular opening.

Moschcowitz² related a very similar finding in a woman of twenty-nine years, who had had cardiac symptoms, palpitation, dyspnoea and occasional oedema of the legs since her fifteenth year, with exacerbation during the last four months, and symptoms of acute infection with chills and septic fever for one week. The blood cultures on one occasion showed *Streptococcus viridans*. At the autopsy both ventricles were hypertrophied, and the right also dilated, and there was a defect in the membranous septum admitting a lead-pencil. The pulmonary valves were replaced by large gray pedunculated vegetations, which extended up the wall of the pulmonary artery to its bifurcation, and had led to multiple emboli in either lung. The prolonged history of cardiac symptoms without adequate cause suggested a congenital lesion upon which the malignant endocarditis had been engrafted.

Dr. W. Thalhimer has sent me photographs of a heart from a cyanotic boy of nine years, with a huge septal defect and pulmonary stenosis in which a vegetative process had developed along the line of closure of the mitral and tricuspid valves. As there was no clinical history of an infective process, no Aschoff bodies in the myocardium, and no evidences of bacteria in the vegetations on microscopic examination, he is inclined to explain the vegetations on the ground of mechanical strain by the unnatural whirls in the blood stream, which have caused microscopic injuries of the valves and have thus given rise to an aseptic thrombosis. From a statistical study of the literature one is led to conclude that, at least in a large proportion of cases, the infective nature of the inflammatory process, so common in the neighborhood of cardiac defects, has been demonstrated.

¹ *Brit. Med. Journ.*, 1897, ii, 1174.

² *Proc. New York Path. Soc.*, 1914, xiv, 18.

In a case reported by Hebb¹ of a girl, aged eighteen years, whose heart showed a funnel-shaped defect at the base of the septum admitting a goose-quill, there were large vegetations on the aortic, mitral, and pulmonary valves, and a *patch of vegetations was also situated on the wall of the right ventricle opposite the defect*. This observation, which is repeated in several other cases, as well as the frequent localization of the vegetations in the right ventricle affords an interesting proof of the fact that under normal conditions the current of blood flows from the left ventricle to the right through the defect. It is natural to suppose that this would be so, for the pressure in the systemic circulation is normally higher than it is in the pulmonary. Further anatomical confirmation of this direction of the stream is afforded by the oblique direction and funnel-shape, with its larger end toward the left ventricle which the opening often assumes, and also by the not infrequent occurrence of patches of fibrosis on the opposite wall of the right ventricle.

Septal defects may exist without producing any change in the heart chambers, but they lead, still more frequently than do defects of the interauricular septum, to hypertrophy and dilatation of both ventricles. Where the defect is combined with *rechtslage* of the aorta, marked hypertrophy of the right ventricle is a constant feature. The pulmonary artery may be markedly dilated, as in 9 cases of the 34 "primary" defects at the base.

The distribution of the auriculoventricular junctional bundle in septal defects is of much interest, and has been investigated by Keith, Mönckeberg, Morison,² and others. As is well known this bundle emerges from the auriculoventricular node close to the interauricular septum behind the medial cusp of the tricuspid valve, and divides into two branches, the left of which pierces the interventricular septum just in front of the pars membranacea, and passes downward superficially beneath the endocardium of the septum to be distributed to the papillary muscles and columnæ carneæ of this chamber, while the right branch runs, more deeply imbedded in the musculature of the right side of the septum, to the apex of the right ventricle. In most of the cases of septal defect examined there was surprisingly little change in this normal arrangement, the fibres streaming over the free border of the septum that formed the base of the defect toward the apices of their respective ventricles. In Morison's case the left branch was abortive. Keith described an abnormal band of "subaortic musculature," which may develop in the pars membranacea and overlies the bundle as it courses down the surface of the septum in the left ventricle, and in one of Mönckeberg's cases of septal defect the bundle lay deeply in the musculature of the left septum instead of sub-endocardially as normally occurs. Recent investigations by Flack and Mall have shown that the interventricular septum is formed, not by a process growing upward from below, as Rokitansky supposed, but by a hollowing out of the spongy musculature of the embryonic ventricle to form the right and left chambers; the tip of the inferior septum, therefore, represents the wall

¹ *Trans. Path. Soc. London*, 1897, xlviii, 41.

² *Jour. Anat. and Physiol.*, 1913, xlvii, 459.

of the lumen of the original cardiac tube, and this may account for the persistence of the bundle at this point in septal defects.

Symptoms and Physical Signs of Septal Defects.—These may be absent and the defect discovered at autopsy. When cyanosis is present it may be slight or transient, appearing only on exertion, or terminal at the end of a long life, or, more rarely, and usually in those cases associated with *rechtslage* of the aorta, it may be well marked. Among the 34 “primary” defects at the base there was an entire absence of cyanosis in 17; it was slight in 5, moderate in 2, marked in 3, and terminal in 4 cases.

Physical signs may also be absent, as in two otherwise normal hearts with defects admitting a goose-quill, in the McGill Museum. On the other hand, physical signs atypical of acquired valvular disease are often present, even in the absence of symptoms, and are frequently sufficiently characteristic to permit of a diagnosis being made. In pronounced cases there may be visible pulsation and precordial bulging, and a thrill, usually systolic in time and diffuse over the precordium, or most marked over the middle of the cardia, is common and is more frequent than in auricular septal defects. A thrill was present in no less than 11 of the 34 cases of primary defects at the base; in 10 being systolic and in 1 a “continuous vibration.” In 7 it was diffused over the whole cardia; in 3 it was most marked over its upper half; in 2 others it was localized at the apex.

A harsh, systolic murmur localized in the third or fourth left space is the most frequent evidence of the defect. Sometimes a very small hole may be accompanied by a very loud murmur. Roger described as characteristic a “single long, constant murmur beginning with systole and continuing through both heart sounds, localized in the upper third of the precordial region.” Reiss mentions as typical a loud systolic murmur in the middle of the precordium, localized over the inner part of the third left space and the fourth rib.

A murmur apparently due to the defect was present in 26 of the 34 cases. In those in which its character was specified it was loud in 18, rough in 3, whistling, grating, harsh, sawing, each in 1, rasping in 3; in 3 instances it was blowing. It was systolic in rhythm in all 26 cases, and in 3 of these a diastolic murmur was present as well. The point of maximum intensity was 12 times in the upper third of the precordium near the left sternal border; of these, in 4 it was stated to be at the third left space, in 2 others also at the fourth left space, in 2 at the third costal cartilage (in 1 of which it was heard with equal intensity at the apex), in 2 at the pulmonary cartilage and second left space, and in 1 “over the middle of the sternum opposite the third left interspace.” Besides these, in 2 other cases it was “along the left sternal border,” “just to the left of the xiphoid cartilage,” and “at the aortic cartilage;” in 2 (in 1 of which it was associated with *rechtslage*) it was “loudest at the apex,” and in 4 it was diffuse over the precordium.

The murmur is usually transmitted downward along the left sternal border, and is frequently heard behind in the left infrascapular region. It may be diffused over the whole precordium, but is usually not heard in the axilla nor below the clavicle. In 6 cases in this series it was so

loud as to be heard over the whole chest, and in 2 cases it could be traced into the vessels of the neck.

Eisenmenger¹ claimed that a systolic murmur produced by the defect may be transmitted along the aorta, and thus be heard in the vessels of the neck, when pulmonary hypoplasia is also present, in which case the blood is diverted by the obstruction from its usual course into this vessel, and so passes from right to left into the aorta. In his own case, diagnosed by Schrötter before death, there was a defect admitting the thumb in the posterior part of the anterior septum, with *rechtslage* of the aorta and a dilated pulmonary artery. The patient, a man aged thirty-two years, had had cyanosis and dyspnoea from birth. There was visible precordial pulsation and bulging, and a systolic murmur over the middle of the heart transmitted everywhere over its surface, but chiefly to the right and inferiorly, not heard above its base, along the course of the aorta nor in the pulmonary artery, the latter vessel being too far below the surface to transmit the sound.

Aneurisms of the Undefended Space.—Cases have been recorded by Rokitansky, Zahn,² Hart,³ MacCallum,⁴ and others, in which, in the absence of any evidence of endocarditis, sacculations, single or multilocular, of the membranous portion of the septum project into the right auricle above the medial cusp of the tricuspid, and in some cases extend also into the musculature of the interventricular septum. Malignant endocarditis of the bulging area is not infrequent and rupture into the right auricle may occur. On this ground it has been argued⁵ that these aneurisms are not of congenital origin, but are due to the action of the inflammatory process upon this delicate part of the septum. As was pointed out by Rokitansky, however, the reverse is probably true, the aneurism supplying a nidus of lowered resistance upon which an infective process has been secondarily engrafted. This point has been made the subject of an interesting communication by Mall,⁶ who pronounces definitely upon the congenital and non-inflammatory origin of these aneurisms, and shows the cause to be a malposition of the inferior septum (inferior septum proper) so that "the membranous septum develops improperly and becomes placed in a horizontal position, and is thus weakened in every way, and predisposed to the formation of aneurisms." In his own case the membranous septum was cribriform, and the hole communicated with numerous sacs in the medial segment of the tricuspid, and also bulged into the right atrium.

Such aneurisms may give rise to marked and characteristic physical signs. This was true of two remarkable cases, one a heart which is in the McGill Museum, the other reported by Tate,⁷ in which a trumpet-shaped tube, which formed the apex of a saccular pouching of the pars membranacea, projected behind and perforated the medial cusp of the tricuspid valve; in the McGill specimen there was malignant endocarditis of the immediately adjacent tricuspid segment.

¹ *Zeitschr. f. klin. Med.*, 1897, xxxii, Supp. Heft, 1.

² *Virchows Arch.*, 1878, lxxii, 206.

³ *Ibid.*, 1905, clxxxii, 51.

⁴ *Johns Hopkins Hosp. Bull.*, 1900, xi, 69.

⁵ *Anat. Record*, June, 1912, p. 2921.

⁶ *Trans. Path. Soc. London*, 1892, xliii, 36.

⁷ *Buhl, Zeits. f. Biol.*, 1880, xvi.

The relative frequency of *aneurisms of the right aortic sinus of Valsalva* and the probable dependence of these upon the juxtaposition of the pars membranacea of the right aortic cusp, has been discussed by Hart.¹ The insertion of the medial cusp of the tricuspid just behind this point may further weaken this region by making it a seat of traction. It is not necessary to presuppose a congenital defect, although this may occur. In a case reported by Hale White² an oval defect admitting a No. 10 catheter lay just below the right half of the anterior aortic cusp: its edges were thickened, but the septum around it for three-quarters of an inch was thin and translucent, and the sinus of Valsalva above it was expanded into an aneurismal pouch, which protruded and burst into the right ventricle. The author thought that the whole septum between the lower part of the aorta and the base of the ventricles was abnormally thin.

Defects in the Septum Elsewhere than at the Base.—These are usually multiple, and irregular or slit-like in form. They are of the greatest rarity. This is especially true of those low down in the septum.

COMPLETE ABSENCE OR RUDIMENTARY DEVELOPMENT OF THE CARDIAC SEPTA.

A rudimentary development of the cardiac septa, leading to a diminution in the number of the heart's cavities, should not be treated entirely apart from localized septal defects, being simply a more extreme degree of the same lesion. Yet the cases may be conveniently grouped together as indicating arrest at a very early stage of embryonic life (fourth week), frequently associated with anomalies elsewhere, and as forming an altogether different and more serious picture.

Cor Biloculare.—Early cases were recorded by Wilson in 1798, Farre in 1814, Ramsbotham in 1846, and Forster in 1847, and there are six in the recent literature by Rudolf,³ Konstantinowitsch,⁴ Gierke,⁵ Schroeder,⁶ Jensen,⁷ and Rivet and Girard.⁸ We have had an opportunity of examining the specimen recorded by Rudolf, which is in the Museum of the Toronto University. The patient was a girl of sixteen years, undeveloped and cyanotic, who suffered from marked dyspnoea and died of pulmonary tuberculosis. The auricular septum was absent and a large right was divided from a smaller left auricular portion, with corresponding auricular appendages, by a slight ridge on the posterior wall. A single large bicuspid auriculoventricular orifice opened into the left side of a single ventricle which gave off a large aorta and a smaller artery from its right side, in transposed relations, and separated from the left part of the cavity by a shallow muscular ridge, which lay in the posterior wall and marked the site of the absent interauricular septum. The pulmonary orifice was stenosed. The cases by Gierke and Konstantinowitsch were

¹ *Virchows Arch.*, 1905, clxxxii, 168.

² *Trans. Path. Soc. London*, 1892, xliii, 34.

³ *Anat. Soc. of Gt. Brit. and Ire.*, Nov., 1899.

⁴ *Prag. Med. Woch.*, 1906, p. 657.

⁵ *Charité-Annalen*, 1908, xxxii, 229.

⁶ *Deut. Arch. f. klin. Med.*, 1911, ccv, 122

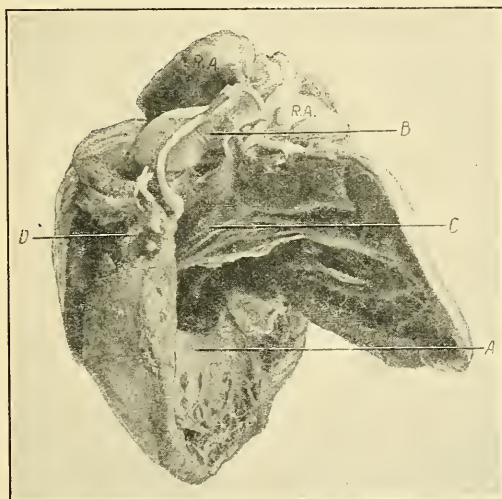
⁷ *Giessen Thesis*, 1912.

⁸ *Arch. des Mal. du Cœur.*, November 11, 1913.

identical with this, except that the great vessels were not transposed and in the former the pulmonary artery was atresic, in the latter the aorta. In other cases the development of the aortic septum was completely arrested and a common arterial trunk replaced the two great vessels.

An anomalous entrance of the pulmonary veins into the superior cava, innominate, hepatic, or other veins, instead of into the left auricle, was noted in Wilson's case, and in most of those recently reported. In that by Rivet and Girard, of a cyanotic infant aged twenty-five days with polycythemia, these veins formed a common trunk which ended in the lobus spigelli of the liver, and anastomosed here with the venæ cavæ and portæ. It seems possible that this anomaly may be the primary one, at least as regards the non-development of the auricular septum, for comparative anatomy shows that differentiation of the auricles is evolved during the formation of a pulmonary circulation.

FIG. 29



"Incomplete double heart," showing (A) the interventricular septum, defective in its upper half; B, a large, thick-walled aorta, arising from both ventricles above the defect; C, a single auriculoventricular cusp arising from both ventricles; D, stenosis of the conus of the pulmonary artery; R.A., the enlarged right auricle. The right auricle and left ventricle are much hypertrophied and dilated; the left auricle and sinus of the right ventricle rudimentary. The interauricular septum is defective in its lower half. (From a specimen in the McGill Pathological Museum, presented by Dr. Andrewes.)

Such cases of pure biloculate heart are extremely rare. A more common form is that in which the septa are partly developed, and an incomplete division has occurred into four cavities, the organ still remaining two-chambered in the exercise of its function (incomplete double heart). A good example is shown in a specimen in the McGill Museum, presented by Dr. F. W. Andrewes (Fig. 29). Here the auricles are incompletely divided into a large right and a small left chamber, by a narrow septum having a large defect above, multiple fenestrations, and a deeply concave lower free border (persistent ostium primum). A thick muscular

septum, one inch high, with rounded free border, projects upward from the lower wall of the ventricle, partly dividing it into a small, thick-walled right, and a capacious left ventricle. A dilated aorta rides above this rudimentary septum and a narrow thin-walled bicuspid pulmonary arises from a rudimentary conus. There is a common auriculoventricular orifice with five cusps, one of which is very strong and large and arises from the opposing wall of either ventricle, stretching across above the rudimentary septum and shielding the auriculoventricular orifice from the two arterial ostia.

A third variation of biloculate or triloculate heart is presented by cases of mitral or tricuspid atresia with absent or defective auricular septum. In tricuspid atresia the ventricular septum has been developed, but a defect remains at the base through which the blood passes from the large left ventricle into the pulmonary artery through the persistent bulbus, the sinus of the right ventricle having become obliterated. An excellent example of the former condition (tricuspid atresia) is published by Robertson¹ under the title, *cor biatriatum triloculare*. The auricular septum was defective below (persistent ostium primum) and an anomalous septum, evidently the persistent right valvula venosa, crossed the right auricle from the Eustachian valve, and was inserted into the base of the interauricular septum at the site of the tricuspid orifice, which was here obliterated, *possibly as a result of the insertion of the anomalous septum at this point*. The great arterial trunks were transposed, the aorta arising from the persistent bulbus arteriosus of the obliterated right ventricle, which communicated with the cavity of the left ventricle by a defect at the base of the otherwise fully developed interventricular septum. Aplasia of the left chambers in mitral atresia is described by Bernstein² and by Girauld and Tissier.³ In the latter's case the left auricle was tiny, and was separated from the left ventricle by a rudimentary bicuspid valve, and a large orifice united it with the greatly dilated right auricle. The right ventricle was also enormous and gave off both the aorta and the pulmonary artery in normal relations but separated from each other by a thick muscular cushion (apparently marking the conus of the pulmonary artery).

Biloculate heart is frequently displaced to the right side of the body, in that type of dextrocardia that is apparently due to arrest of development. It is often associated with transposition of one or more viscera or other serious defects. The spleen was absent in three of the cases.

Cor Biatriatum Triloculare.—Absence of the ventricular with presence of the auricular septum constitutes a three-chambered heart with two auricles and the tricuspid and mitral orifices opening into a common ventricle, from which (if the aortic septum develops), two arterial trunks arise. Arnold⁴ reports a case of complete absence of the ventricular septum, with auricular septum defective below (persistent ostium primum), pulmonary atresia, dextrocardia, and absence of the spleen, and adds a study of 30 cases of *cor biatriatum triloculare*. As in *cor*

¹ *Lancet*, 1911, 180, p. 872.

² *Proc. New York Path. Soc.*, 1906, N. S., vi, p. 29.

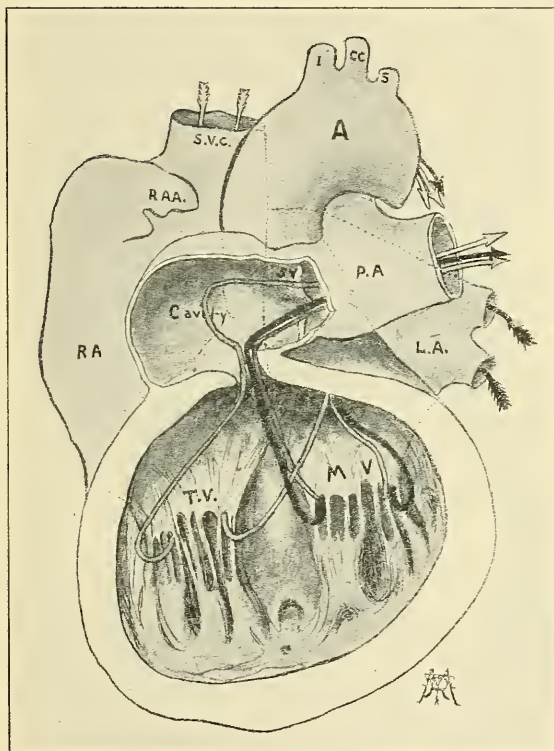
³ *Bull. Soc. d'Obstet. de Paris*, 1910, xiii, 420.

⁴ *Virchows Arch.*, xlii.

bilocular, obliteration of the right ventricle in tricuspid atresia (with auricular septum present) is frequently reported as trilobulate heart.

A special type of anomaly has been established, of what is functionally a cor biatriatum trilobulare, although four chambers exist, by a series of cases recorded in which an anomalous septum cuts off from a common ventricle a small chamber which lies at the base of the heart and gives off one or the other of the great arterial trunks. Such a case, reported and figured by Holmes,¹ in 1824, the specimen from which is in the McGill

FIG. 30



Cor biatriatum trilobulare with malposed interventricular septum. Diagrammatic sketch by Prof. R. Tait Mackenzie, showing course of blood and relation of cavities in Dr. Andrew Holmes' case of displaced interventricular septum cutting off a small cavity which gives off the pulmonary artery. The pale line shows venous, the dark line arterial blood. (From the Medical Museum of McGill University.)

Museum, is represented diagrammatically in Fig. 30. The auricles, which were enormously dilated, especially the right, emptied their contents through their respective ostia into a common ventricle, which gave off the aorta behind and somewhat to the left and communicated through a diamond shaped opening in an anomalous septum with a small cavity at its right upper angle of the common ventricle which gave off the dilated pulmonary artery in its normal relation to the aorta. In eight

¹ *Edin. Med. Chir. Soc.*, 1824, republished by M. E. Abbott, *Montreal Med. Jour.*, 1901.

other similar cases reported by Young,¹ Peacock,² Rokitsky (2 cases), Chiari, Thérémín (Obs. 43), and Marchand,³ and in a specimen which the writer has had the privilege of studying in the Museum of the Harvard Medical School, the aorta arose from the small chamber in front and to the right, and the pulmonary artery from the common ventricle behind it, the two vessels being in transposed relations. It has been suggested by Keith that in these cases the anomalous septum is the persistent lower orifice of the embryonic bulbus cordis, but study of both the McGill and Harvard specimens lead us to the conclusion, that in these specimens, at least, the strong muscular wall with a large defect at its upper border through which the small cavity communicates with the large common ventricle, is simply the malposed interventricular septum itself, which has failed to unite with the aortic septum, and has been carried around to the right in the further development of the heart.

Cor Biventriculare Triloculare.—When the auricular septum is absent and the ventricular septum present, a heart with two ventricles and a single auricle results. Such a case is reported by Williams.⁴ All the blood entered the common auricle through the superior vena cava (the pulmonary veins having again an anomalous entrance).

Symptoms and Physical Signs.—In biloculate heart cyanosis is usually present from birth, and becomes very marked. The cases of Forster,⁵ Ramsbotham,⁶ and Crisp⁷ were all typical morbus cæruleus, dying, respectively, at seventy-eight hours, ten days and ten weeks. On the other hand symptoms may be moderate, as in Turner's case, in which there was no cyanosis until just before death at the age of fifteen months. Cases of cor biatriatum triloculare present perhaps the best illustrations we have that the admixture of venous and arterial blood is compatible with long life and with only slight disturbances of the circulation. Young's patient, who died at thirty-nine years, cyanosis having developed only within the last three weeks of life, and Peacock's almost identical case, already noted, and that by Mann,⁸ dying at twenty-one years, are illustrations. Holmes' specimen (Fig. 30) was from a young man, aged twenty-four years, in whom there was only moderate cyanosis and a tendency to suffocative attacks. Physical signs may be prominent, but cannot be said to be characteristic.

DEFECTS OF THE AORTIC SEPTUM.

When the aortic septum fails to develop, a single large thick-walled trunk (*persistent truncus arteriosus*) results, which arches upward in the course and gives off the branches of the normal aorta, the pulmonary artery arising therefrom. This abnormality is very uncommon. Partial defect of the aortic septum is even less frequent than is its complete absence. It may result in a common trunk with early division into aorta

¹ *Jour. Anat. and Physiol.*, 1907, xli, 190.

² *Trans. Path. Soc.*, London, 1854, vi, 177.

³ *Verh. d. XII Deut. path. Gesell.*, 1908, p. 174.

⁴ *Jour. Anat. and Physiol.*, 1894, xxviii, 305.

⁵ *Trans. Path. Soc.*, 1846, i, 21.

⁷ *Trans. Path. Soc.*, London, 1859, x, 49.

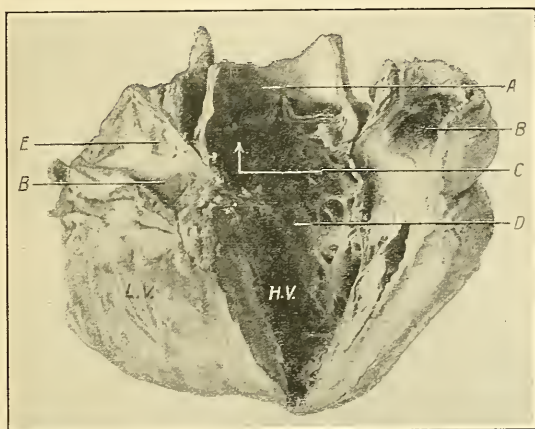
⁶ *Ibid.*, p. 21.

⁸ *Ziegler's Beitr.*, 1889, vi, 485.

and pulmonary artery and rudimentary septum within it, or, when the defect is still smaller, in an abnormal communication between the aorta and the pulmonary artery or the conus of the right ventricle.

Persistent Truncus Arteriosus (Common Arterial Trunk, Complete Defect of the Aortic Septum).—This abnormality is very uncommon, only 22 cases are available in the literature and from other sources of study. The cardiac septa are frequently rudimentary or absent, a biloculate or triloculate heart existing. When, however, these are well developed and the heart is four-chambered and otherwise normal, a localized defect at the base of the interventricular septum always remains. The common trunk either rides above it, receiving the blood equally from both ventricles, or arises more or less entirely from the right ventricle, the blood entering it from the left through the defect.

FIG. 31



Persistent truncus arteriosus. Heart of a child, aged five years, in whom cyanosis developed at one and one-half years. *A*, common arterial trunk arising entirely from right ventricle, and communicating with the left ventricle through the right auricle; *B*, right auricle laid open; *C*, defect at base of interventricular septum; *D*, heavy muscular column from wall of right ventricle to base of defect; *E*, interauricular septum seen from right auricle showing multiple defects. Heart is wider than high. (From a specimen in the McGill Pathological Museum presented by Dr. Mackenzie Forbes.)

This recalls the early stage at which the arrest of growth has occurred, when the primitive aorta is given off entirely from the right side of the common ventricle (Fig. 16). A typical specimen of this kind is shown in Fig. 31 from a specimen in the McGill Museum. The large common arterial trunk springs entirely from the right ventricle, and has three strong semilunar cusps, behind two of which the coronaries arise. Below the anterior and right posterior cusps there lies a circular defect in the septum, admitting the little finger, with rounded edges, by which the left ventricle communicated with the aorta and with the right ventricle, which is much hypertrophied; a heavy muscular column runs from the anterior wall of this ventricle to the lower border of the defect. The left auricle and ventricle are perfectly formed, but are much smaller than the right chambers. There are multiple defects in the interauricular septum. The blood supply to the lungs is unknown.

The pulmonary circulation in these cases is of the greatest interest. Two large branches, one to either lung, may arise from the wall of the common trunk some distance above its origin, as in the cases of Heath¹ and Ramsbotham. Quite commonly one pulmonary branch arises from the aorta soon after its origin, and supplies either the right or the left lung, and a second branch passes to the lung of the opposite side from the descending aorta, the first vessel evidently representing the pulmonary portion of the truncus (sixth aortic arch) and the second the patent arterial duct. This occurred in Dickson's² and Wirth's³ cases, and also in that by Preisz.⁴ In the latter, distinct traces of a partial development of the aortic septum were apparent. A common trunk provided with four semilunar cusps, 14 mm. in diameter, arose from the right ventricle above a large septal defect, and widened rapidly to 3 cm., becoming grooved externally to indicate the right and left portions of its lumen, that part on the right giving off the vessels of the arch, and thus representing the aorta, while that on the left yielded the vessels to the right lung and represented the pulmonary artery. An additional pulmonary artery was here also sent to the lungs from the descending aorta in the position of the ductus arteriosus.

In a few instances in which the defect in the aortic septum appears to be only partial, the common trunk divides immediately after its origin from the heart, two-thirds of its lumen on the right forming the aorta, and one-third on the left forming the pulmonary artery, which takes its normal course.

This early division occurs in both of Rokitsansky's cases, and in them the partial character of the defect is also proved by the presence of a delicate sickle-shaped septum within the undivided portion of the trunk, joining its wall between the left and posterior semilunar cusps behind, and left and right cusps in front. In Clarke's⁵ case the trunk divided early, but there was no sign of a rudimentary septum within.

The above are examples of true *persistent truncus arteriosus*. Under this title is also reported a series of cases in which the single trunk passing from the heart, represents the greatly dilated aorta or pulmonary artery, as the case may be, and an atresic cord attached to the external surface of the heart *represents the obliterated origin* of the other vessel. In one of Farre's cases, for instance, and in one by Forster, the single large trunk represented the pulmonary artery, and "a single coronary vessel which descended from the concavity of the arch to the base of the heart where it divided into two coronary arteries" was evidently the aorta, which was atresic at its origin, and was connected with the pulmonary by a large patent ductus. In Crisp's case, on the other hand, the pulmonary artery was rudimentary, and the large trunk represented the aorta.

As pointed out by Gierke, and also by Wirth, such cases should be clearly distinguished from the true persistent truncus due to complete absence of the aortic septum. Where the interventricular septum is

¹ *Trans. Path. Soc.*, London, 1864, xii, 62.

² *Jour. Anat. and Physiol.*, 1914, xlviii, p. 210.

³ *Giessen Thesis*, 1912.

⁴ *Ziegler's Beiträge*, 1890, vii, 247.

⁵ *Trans. Path. Soc.*, London, 1885, xxvi, 178.

defective at its base, as it is in all these cases, there is a tendency for the aortic septum to develop irregularly, thus cutting off a narrow aorta or pulmonary artery, as the case may be, and the calibre of the smaller vessel is likely to become still further reduced in size by the passage of the bulk of the circulation into the larger trunk. For this reason obliteration of one trunk in biloculate heart where no interventricular septum is present, is a comparatively common event, and the cases should be sharply distinguished from a true defect of the aortic septum. Gierke suggests that the presence of four semilunar cusps such as occurred in Preisz's case is positive proof of an undivided primitive arterial trunk, while the presence of three semilunar cusps such as occurred in the McGill specimen, his own, Dickon's, and Wirth's argues that development of the aortic septum had occurred and that obliteration of one or other of the vessels had taken place as a secondary event.

Symptoms and Physical Signs.—Much the same remarks apply to persistent truncus as to bilocular heart, for symptoms and signs are not always commensurate with the seriousness of the lesion. But here the condition is a still graver one and the average duration of life is much shorter. Crisp's patient, a girl dumb from birth, with only slight cyanosis and clubbing, lived to twelve years, Forbes' to five years, Peacock's to thirteen months, and Buchanan's, who had a four-chambered heart with defect at the base of the septum, giving physical signs but no cyanosis, to six and a half months; all the others were marked cases of *morbus cæruleus* and died at birth or in early infancy. Vierordt quoted one dying at sixteen and another at nineteen years.

Communication between the Aorta and Pulmonary Artery.—(**Partial Defect of the Aortic Septum.**)—A few cases have been described in which a circular or oval hole with perfectly smooth edges, and evidently not of inflammatory origin lies in the anterior wall of the aorta a short distance above the semilunar cusps, and leads directly into the pulmonary artery shortly above its origin. A valuable developmental study was made by Hektoen,¹ who gives a case of much interest and collected 9 others from the literature.

The effect produced upon the circulation by the abnormal communication between the two great vessels is the same as in a patent ductus arteriosus, but the two conditions are quite distinct and have an entirely different etiology. This lesion is not a patent ductus abnormally shortened so that aorta and pulmonary artery have been approximated, with an apparent hole as a result. It is a true defect, as is proved both by its situation, which is much nearer to the origin of both arteries than is the ductus, and by the fact that in several of the cases reported the ductus has been present as well. Neither is the defect of an inflammatory nature, as is well seen in the smooth condition of its edges in the cases of Girard, Wilks, and Rickards, and from the character of the combined defects in the latter and in Fraentzel's case.

The abnormal opening is clearly a partial defect of the aortic septum, not at its junction with the interventricular septum, but higher up in

¹ *Trans. Chicago Path. Soc.*, 1905.

its own substance, probably at the point where the distal bulbar swellings meet the aortic septum proper in the embryo.

In all the recorded cases but one, the hole lay in the aortic wall a short distance above the semilunar cusps. In that of Rickards the aortic valve was bicuspid, and its segments congenitally fused. A funnel-shaped opening communicated with the pulmonary artery and lay behind the larger (fused) cusp. A triangular defect in the interventricular septum existed also in this case.

Instead of opening into the pulmonary artery, the hole may lead from the aorta into the right ventricle as in the cases of Livingstone¹ and Cayla. In one of Hektoen's cases the anomalous opening led from the aorta into the right ventricle through a defect at the base of one of the semilunar valves. This, also, is a most interesting example of a defect of the lower (bulbar) part of the aortic septum.

A *communication* between the aorta and pulmonary artery of an *acquired nature* may occur in much the same situation as in the congenital form in aneurism of the base of the aorta. There is quite a large series of cases, especially in the earlier literature, which is reviewed by Brocq.² The congenital cases are to be distinguished from those due to perforation of an aneurismal sac by the smooth appearance of the edges of the opening and the healthy arterial wall. The physical signs produced are the same and are often of remarkable intensity. Gairdner³ reported a typical case, characterized by a continuous murmur.

The pulmonary artery was larger than the aorta in Wilks' and Rickard's cases, a little smaller in Fraentzel's and Girard's cases. Marked hypertrophy and dilatation of all the chambers of the heart, especially of the right ventricle, constantly results. In Girard's and Rickards' cases, in which there was no other cardiac lesion, the hearts weighed, respectively, 670 gms. and 23 oz. (651.8 gm.).

Symptoms and Physical Signs.—Cyanosis is not, as a rule, present, and there is no characteristic picture, excepting that obstruction to the circulation is clearly manifest. All the cases recorded died before middle life with anasarca and other symptoms of chronic heart disease; those of Girard, Rickards, and Fraentzel reached thirty-seven, thirty, and twenty-five years respectively. Wilks' infant died at eight months, Hektoen's and Lebederber's at birth. Precordial discomfort, amounting often to actual distress, was present since childhood in Rickards' patient, as also in Fraentzel's and Girard's, and in the two latter there was dyspnoea on exertion and slight cyanosis. Physical signs may be absent or may be very marked, and they may vary, being sometimes quite atypical, or sometimes those usually associated with a patent ductus arteriosus. Owing to the great hypertrophy of the heart the cardiac dulness is usually much increased, especially to the right, and there is precordial bulging. Girard's case was characterized by a slight thrill and systolic murmur at the apex, which latter gave place later to reduplication of the first sound and distinct gallop rhythm.

¹ *New York Med. Rec.*, 1883, p. 249.

² *Revue de méd.*, 1885, v, 1046 and 1886; vi, 786.

³ *Glasgow Hospital Reports*, 1899.

A diastolic murmur is common. In Rickards' case the cardiac dulness was enormously increased, and there was an intense purring double thrill over the cardia, and murmurs, systolic and diastolic, running into each other, were heard over the whole front and back of the chest, so loud as to be audible even through the bedclothes. In Fraentzel's patient, in whom there was a gaping opening 12 mm. across between the two vessels, and the right pulmonary artery arose from the ascending aorta, the heart was found to be greatly enlarged; both sounds were heard at all the ostia, and a systolic murmur was heard at the apex; in the fourth left space near the sternal border was a loud systolic and a long diastolic murmur, the latter heard with equal intensity over the base of the xiphoid cartilage. Both sounds and a diastolic murmur were audible in both second spaces, the murmur being louder and rougher in the second right space than in the left. Both sounds as well as systolic and diastolic murmurs were audible in the carotids.

DEVIATION OF THE AORTIC SEPTUM.

According to the teaching of Rokitansky, transposition of the arterial trunks, *Rechtslage* or deviation to the right of the aorta, as well as certain developmental forms of pulmonary and aortic stenosis, are due to irregularities in the development of the septum within the aortic bulb, or to its malunion with the interventricular septum. As this theory with certain modifications still finds general acceptance, the cases embraced by it will be considered here.

Transposition of the Arterial Trunks.—This may be defined as an alteration in the position of the two great vessels relative to the ventricles of the heart or to each other at their origin, so that they either spring from reversed ventricles, the aorta from the right and the pulmonary from the left chamber (complete transposition), or from the ventricle to which they normally belong, but in a reversed relationship ("corrected" transposition).

The condition was first described by Baillie in 1797, and early cases were reported by Farre in 1814, Ward¹ in 1851, Peacock² in 1854, Buchanan³ and Meyer⁴ in 1857, Cockle⁵ in 1863, and Kelley⁶ in 1870. As a result of systematic observation of the autopsy material of infants at the St. Petersburg Foundling Hospital, Thérémín found 26 cases of transposition among 106 cardiac defects. In his summary of the literature in 1898, Vierordt mentions (p. 47) 76 cases of transposition among 383 cardiac defects analyzed. Some thirty additional cases have been reported since. Among 270 cardiac defects in the London Museums examined by Keith, transposition occurred in twenty-five. In our series of defects it was present seventy times.

Pathogenesis.—Peacock and others ascribed this anomaly to an irregularity in the development of the aortic septum, but until Rokitansky's

¹ *Trans. Path. Soc.*, London, 1851, v, 67.

² *Ibid.*, 1854, vi, 117.

⁴ *Virchows Arch.*, 1857, xii, 364.

⁶ *Trans. Path. Soc.*, London, 1871, xxii, 92.

³ *Ibid.*, 1857, viii, 149.

⁵ *Medico-Chir. Trans.*, 1863, xlii, 193.

work appeared in 1875, it remained a little understood phenomenon. In some minor particulars the observations of Rokitsansky upon development do not coincide with those of later observers, but it is in the elucidation of the complex and hitherto obscure subject of transposition of the arterial trunks that the value of his great achievement may be said chiefly to lie. Rokitsansky's explanation of transposition is one of those revelations, astonishing by its simplicity, and, as Vierordt remarks, he had the singular triumph of having supplied a working hypothesis that has not only explained the facts of his own experience, but has outlined and foreseen other pathological possibilities which have since been realized. He described and figured sixteen different forms of transposition, due, he believed, to different degrees and combinations of deviation or malunion of the aortic and interventricular septa, some of which he himself observed, and others have since been recorded by later workers. Even if the advance of comparative embryology should unfold some other explanation of this subject, the verification of Rokitsansky's brilliant hypothesis by the subsequent observation of different forms of transposition shown by it to be possible, indicates that, so far as it goes, his theory is true, and that growing knowledge will amplify rather than supersede his solution of this difficult problem.

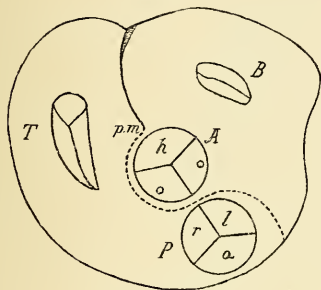
Since the above statement was written for the first edition of this work, a remarkably clear exposition of Rokitsansky's theory in the light of recent investigations upon the normal anatomy of the bulbus cordis in the dipnoan and reptilian heart and in the mammalian embryo, has been published by Jane Robertson.¹ The following is a brief statement of Rokitsansky's doctrine of transposition, as corroborated and amplified by the result of these researches.

As may be seen by a glance at the normal adult heart, the great trunks normally undergo a distinct torsion upon each other just above their origin, so that the pulmonary artery, which arises in front and to the left, passes back behind the ascending aorta to the lungs, while the aorta, although coming to lie ventral to the pulmonary artery, springs from the heart behind it and to the right. This torsion of the vessels is represented in the bulbus cordis of the early embryo and in the dipnoan fish by a spiral arrangement of the valvular endocardial folds of the bulbus cordis, which results from a kinking upon itself of the bulbus, which structure was at an earlier stage a straight tube. The aortic septum is formed in its proximal portion by fusion of the spirally placed endocardial ridges of the bulbus cordis, and in its distal part by a growth downward of a septum in the common arterial trunk. If for any reason this normal kinking does not occur and the bulbus remains a straight tube, the aortic septum will not assume its spiral form, and the normal torsion of the great trunks upon each other cannot take place. The result is an aorta arising anteriorly and passing directly upward to the arch, and a pulmonary artery arising posteriorly and passing directly backward to the lungs, *i. e.*, *transposition*. In other words, transposition of the arterial trunks is due to a lack of development of the torsion that normally

¹ *Jour. Path. and Bacteriol.*, 1913, xviii, 191.

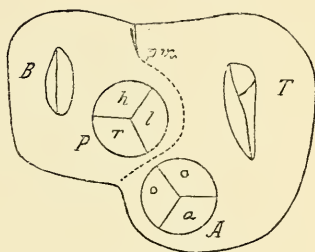
occurs. The transposed vessels may be placed in their proper ventricles in spite of their relative displacement, by the sympathetic adjustment of the aortic in its union with the interventricular septum. In this case the transposition is "corrected" (Rokitansky's Scheme A). Or the transposed vessels may be placed in the *reversed* ventricles by the union of the interventricular with the proximal portion of the malposed aortic septum, when "*uncorrected*" (*anomalous*) *transposition* results (Rokitansky's Scheme B).

FIG 32



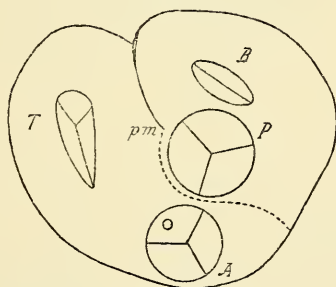
Normal relation.

FIG. 33



Corrected transposition

FIG. 34



True complete transposition, vessels in reversed ventricles.

A, aorta; P, pulmonary artery; T, tricuspid valve; B, bicuspid valve; pm, pars membranacea: p, posterior cusp; a, anterior cusp; lr, left, right cusps (the small circles indicate the situation of the coronary article.) (Republished from Vierordt, Nothnagel's System, 1898, xv, 1, 2.)

Rokitansky recognized this spiral disposition of the aortic septum and taught that these two factors, a deviation of the septum within the aortic bulb and its faulty union with the interventricular septum, might occur in all degrees and combinations, giving rise to a corresponding number of different forms of displacement of the arterial trunks or of "corrections" of such displacements. He distinguished two main classes (according as the transposition is "corrected" or otherwise by the interventricular septum), with eight sub-varieties in each. Of these his "Scheme A" has as its type or starting point the normal relation, in which the concavity of the septum looks backward and to the right. The different subvarieties are constituted by the different degrees of

deviation of the aortic septum rotating in an imaginary circle from right to left. The characteristic of the group as a whole is that the interventricular unites with the aortic septum in such a way that, although the trunks are altered in their relation to each other, they remain placed in their respective ventricles: that is to say, the transposition is "*corrected*."

In his second group, or "Schema B," on the other hand, the arteries arise throughout from the "reversed" ventricles; that is to say, the transposition is "*uncorrected*" in the union of the interventricular septum. The type, or fundamental form from which the series starts, is the so-called *transpositio vera*, in which the septum has rotated through 180 degrees, so that its concavity looks downward and to the left, and the arteries lie in reversed cavities in the exact opposite of the normal position, the aorta to the left and anteriorly, the pulmonary to the right and posteriorly (Fig. 34). Another explanation of transposition has been offered recently by Keith, namely, that it is due to an atrophy of the bulbus cordis around the pulmonary artery, and its great muscular development about the origin of the aorta, where it normally undergoes involution. The effect would be the pulling round of the aorta at its orifice to the position normally occupied by the pulmonary artery, so that the relation of the two vessels to the auricular canal becomes reversed.

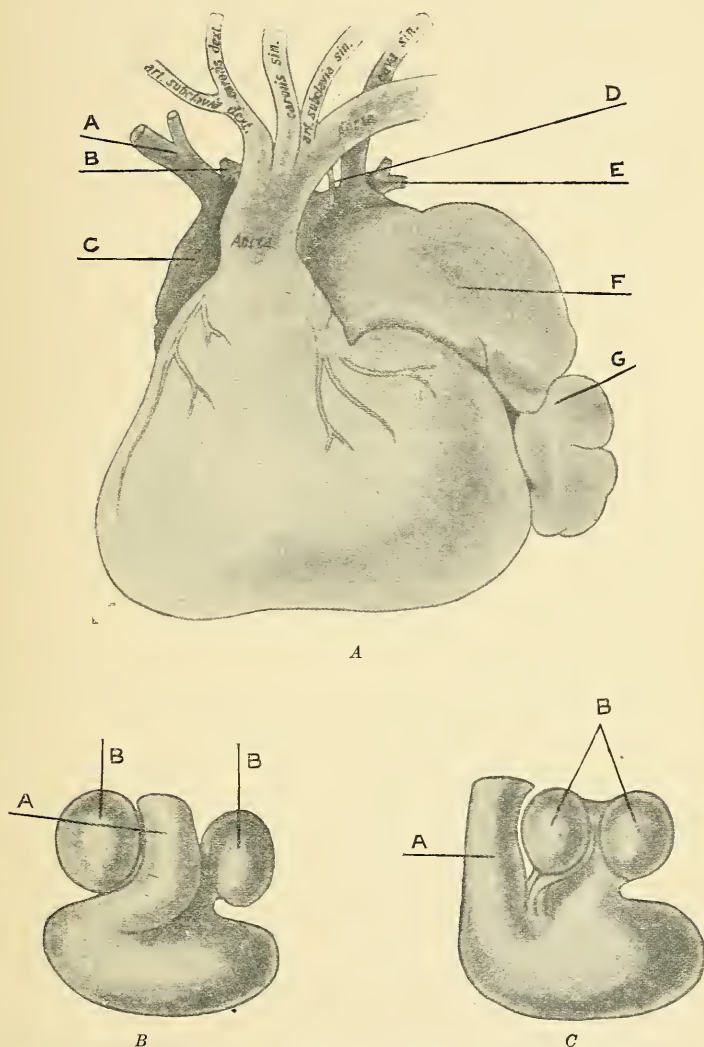
A similar result would be attained by supposing a reversal of the normal right to left bulboventricular bend, so that this undergoes a left to right twist, which would bring the vessel lying posteriorly into relation with the right side of the auricular canal. Such a reversal of the bulboventricular bend has been suggested to me by Dr. Lewis as a probable explanation of those cases of transposition in which the transposed aorta is cut off by an anomalous septum from a common ventricle, and has also been mentioned in this connection by Keith.

From a consideration of the above theories, and from the study of two models made by Dr. Frederic Lewis and myself, the series of events occurring in transposition appears to us to be as follows: (1) A reversal of the bulboventricular bend, so that the two great trunks resulting from division of its distal aortic portion come to occupy a reversed relation to the auricular canal; (2) a reversal of the normal kinking of the aortic bulb so that it remains a straight tube or assumes a curve complementary to the reversed bulboventricular twist below; (3) a consequent reversal of the normal spiral arrangement of the bulbar endocardial ridges; and (4) a resulting malposition of the aortic septum so that its spiral twisting either does not take place, or takes place in a reversed direction, leading to a lack of the normal torsion of the great arterial trunks, that is, *transposition*.

The interdependence of the first and second of the above events is evident from a glance at the compensatory curves of the normal embryonic bulbus (Plate V), but the question as to which of these two is of primary occurrence is not altogether clear. The reversal of the bulboventricular twist may be of the nature of a localized *situs inversus* and the causative factor of the whole proceeding. Or it may be secondary to a primary arrest of the kinking that normally takes place in the aortic bulbus, and of the consequent lack of spiral disposition of its valves.

That the second of these two alternatives, namely, a primary arrest of development, may be the correct solution is suggested in a striking

FIG. 35



A, Wenner's case of cor biatrium triloculare with transposed aorta and pulmonary artery passing up to the right, and both right and left auricular appendages displaced to the left side. A, Superior vena cava; B, right pulmonary artery; C, right auricle; D, ductus botalli; E, left pulmonary artery; F, right auricular appendix; G, left auricular appendix.

B, figure of normal embryonic heart showing the position which the truncus comes to occupy between the auricular appendages after the normal shunting to the left of this structure has taken place. A, common arterial trunk; B, B, auricular appendages.

C, figure of embryonic heart in which the normal shunting to the left of the common arterial trunk has not occurred, so that this structure still comes off entirely from the right side of the heart (as in the very early stages), and both auricular appendages still lie on the left (as in Wenner's case). A, common arterial trunk; B, auricular appendages. From *Beiträge zur Lehre der Herzmissbildungen*, Case 9. Otto Wenner, *Virch. Arch.*, 1909, 196, pp 140, 155.

way by two remarkable cases reported by Wenner,¹ and Birmingham² of "pure" dextrocardia, in which the transposed vessels arose from the extreme right side of a common (in Birmingham's case of a right) ventricle, and *both auricular appendages lay entirely on their left side*, just as in the very early embryo, the common auricle lies to the left of the common trunk. In both cases the dextrocardia was not a true situs inversus, but the apex of the heart was formed by the right ventricle, again evidencing a persistence of an early embryonic state, and a true primary arrest of development.

Pathology.—It is impossible to follow Rokitansky's minute classification in a statistical study of recorded cases, for the relation of the vessels to each other is often indefinitely stated. For practical purposes the classification into complete, corrected, and partial transposition, suggested by Vierordt, may be used.

(a) In *complete transposition*, the vessels arise from reversed ventricles. This occurred in 43 of our 70 cases. In 18 of these the aorta arose from the right ventricle to the right and in front, and the pulmonary artery to the left and behind. The so-called *transpositio vera*, in which the aorta arises in exactly reversed relation to the left and anteriorly, and the pulmonary artery from the left ventricle to the right and posteriorly, is illustrated by the cases of Pye-Smith³ and Thiele. The pulmonary rose above a defect in the septum and the aorta from the infundibulum of the right ventricle in three of Thérémín's cases, and in those of Lees and Rheiner. The aorta rose from both ventricles above the defect, the pulmonary from the left ventricle, in that by Buchanan.⁴

(b) In *corrected transposition* (see Fig. 33 Scheme A). the relation of the vessels to each other is altered, but they are placed in their proper ventricles by the union of the interventricular septum. Minor degrees of displacement probably often pass unnoticed, for the "correction" prevents pathological results. More extreme grades can be at once recognized. Six almost identical cases are described by Rokitansky (two cases), Rauchfuss, Tonnies,⁵ and Thérémín (two cases), in which the aorta and pulmonary artery are completely reversed in relation to each other, but arise each from their own ventricle. In all there was a defect in the interventricular septum at the base, and in all *the auriculo-ventricular orifices were also transposed*, the mitral lying in the right, the tricuspid in the left ventricle, and thus the "correction" of the transposition of the arteries by the septum was seemingly nullified; the aorta arises from a ventricle of venous form (in that it has a tricuspid valve), the pulmonary from an arterially constructed one. Rokitansky suggests that in these cases "the ventricle in which the septum arises anteriorly forms as the arterial one." Fingerhuth described a case of corrected transposition with situs inversus of the viscera, and no transposition of the ventricles.

¹ *Virchows. Arch.*, 1909, xcvi, 127.

² *Jour. Anat. and Physiol.*, 1893, xxvii, 139.

³ *Trans. Path. Soc.*, London, 1873, xxiii, 80.

⁴ *Ibid.*, 1857, viii, 149.

⁵ *Göttingen Thesis*, 1884.

(c) *Partial transposition*, in which both vessels arise from the same ventricle or from a common ventricle in reversed relations, is relatively infrequent. *Both vessels may arise from the right ventricle*, as in Thérémín's forty-first observation and in Tooth's case,¹ in which a large thick-walled aorta arose from the usual origin of the pulmonary artery, which was itself small, thin-walled, bicuspid, and was given off from the right ventricle directly behind the aorta. *Both vessels may spring from the left ventricle*. Thus, Crocker reported a girl, aged thirteen years, in whom the pulmonary artery, small and constricted, arose from a small, thick-walled, left ventricle to the right and anteriorly, while the aorta arose from the same cavity posteriorly, and communicated with the right ventricle through a defect in the septum. *Both vessels may arise transposed from a common ventricle*, as in two examples of cor biatriatum triloculare with pulmonary atresia and transposition, and in the biloculate heart reported by Rudolf. The remarkable cases of displacement of both auricular appendages to the left of the transposed vessels fall in this category. Finally, the transposed vessels may arise from a rudimentary cavity cut off by an anomalous septum from the common ventricle.

The condition of the semilunar cusps in transposition is of interest. In one or other of the vessels, more commonly in the pulmonary, they are frequently deformed, of unequal length, bicuspid, or, as in Bokay's case, markedly increased in depth. Their position varies with the degree of displacement, and should therefore be carefully observed, as the degree of deviation may be thus detected. In true transposition, for instance, the non-coronary cusp in the aorta lies anteriorly instead of posteriorly.

Changes in the relative size and thickness of the two great trunks are usually present, and are of importance as supporting Rokitansky's view that an altered position of the aortic septum is a fundamental part of the condition. In spite of the fact that the pulmonary arises from the left ventricle, which is anatomically constructed as the strongest of the two chambers, this vessel is usually thin-walled and narrowed and its orifice is stenosed or atresic, while the aorta is dilated. Among Rokitansky's 18 cases of transposition, pulmonary stenosis or atresia occurred 11 times, and it was present in 17 out of the 25 cases of Keith's series. In a few instances the reverse holds good and a large thick-walled pulmonary may be combined with a short, narrow aorta. Thérémín's series of 14 cases in infants, 10 of which were of complete and 4 of partial transposition, forms a remarkable exception to the above statement. In 3 of his cases the pulmonary was dilated, and in the remainder it was equal in size to the aorta. In our own series, which includes these 14 of Thérémín's, among 70 cases, in 43 of which the transposition was complete, in 22 partial, and in 5 "corrected," the pulmonary was stenosed or atresic in 23 cases.

The Fetal Passages.—In complete transposition the venous blood from the right heart is distributed to the arterial system through the aorta, while the aërated blood entering the left auricle is returned again

¹ *Trans. Path. Soc.*, London, 1879, xxxi, 92.

to the lungs by the pulmonary artery. The conditions of the circulation are thus of the poorest, and unless one or other of the fetal passages remains open, life cannot be sustained. The interventricular septum is frequently entire, but a widely patent foramen ovale is nearly always present and combines with a patent ductus or with a septal defect to allow of the passage into the aorta of the aërated blood. Very rarely does one of these conditions exist singly. In our series, among 37 cases of complete transposition the foramen ovale was patent 32 and the ductus arteriosus 22 times. A patent foramen was the only communication between the two sides of the heart in 8 cases, namely, those by Emanuel, Dorning,¹ Kelly, Cockle, Bokay, and in three of Thérémin's cases. It was combined with a patent ductus in 14 cases, with a defect of the interventricular septum in 6, and with patency of both of these openings in 4 cases. The ventricular septum was completely closed in 25 cases and was defective in 12, in one of which, that by Heuyer and Campergne,² the septal defect was the only communication, and in another by Guttman³ the ductus arteriosus was also patent. In Thérémin's thirty-seventh observation and in Ramm's case, a large patent ductus was the only communication between the right and left heart. In a few cases the bronchial arteries were markedly dilated.

Bokay⁴ has made an analysis of 43 cases of complete transposition, with regard to the condition of the fetal passages, and there are 33 additional cases in our series from the literature. The following table shows the condition of the fetal passages in these 76 cases.

	F. O. Patent.	D. A. Patent.	V. S. Defect.
F. O. patent	16	36	7
D. A. patent	36	3	3
V. S. defect	7	3	5
Patent F. O., defect V. S., patent D. A.	4	4	4
Total	63	46	19

The abbreviations are as follows: F. O., foramen ovale; D. A., ductus arteriosus; V. S., interventricular septum.

Hypertrophy and Dilatation of the Heart.—Under the altered conditions of the circulation the aorta is required to supply blood, not only to the systemic circulation, but through one or other of the persistent fetal passages to the lung. The right heart is practically invariably hypertrophied and dilated, sometimes to an enormous extent, and the right auricle likewise. The left chambers usually share in these changes though to a less degree.

Symptoms and Physical Signs.—During the period of fetal circulation, transposition of the vessels is of little pathological significance, so that, unless associated anomalies exist, the subjects are born at full term, well developed, and apparently normal. In complete transposition, marked

¹ *Trans. Am. Ped. Soc.*, 1891, ii, 46.

² *Bull. de la Soc. Anat.*, April, 1913, p. 209.

³ *Deut. med. Woch.*, 1893, xc, 74.

⁴ *Arch. f. Kinderheilk.*, 1911, lv, 321.

cyanosis is almost always a prominent feature, but it may not be present at birth, appearing usually after some days or weeks, and perhaps developing, as Thérémín suggests, as the ductus becomes obliterated. On account of the extreme degree of the cyanosis, clubbing of the fingers and toes usually develops in infants which have survived the first six months of life. In partial transposition, on the other hand, or in complete transposition with large septal defects, cyanosis may be quite moderate in degree. In Thérémín's patient, dying at three and a half years, there was no cyanosis until the last illness, but large defects of interauricular and interventricular septa combined to relieve the situation. In a remarkable case of partial transposition, recorded by Lebert,¹ death occurred from failing compensation, at the age of twenty, without any sign of cyanosis having developed during life. The patient was a young man in good health until three years previously, when cardiac symptoms developed suddenly after lifting a heavy weight. The aorta arose in front of the pulmonary from the right ventricle, the pulmonary was stenosed and a large septal defect admitted the index finger.

In uncomplicated cases, and where a ventricular septal defect is either not present or is of small size, *physical examination may yield no evidence of the defect*, except a sharply accentuated second sound over the pulmonary (aortic) area. The combination of marked cyanosis with signs of hypertrophy of the right heart and an entire absence of adventitious sounds, or precordial thrill, in an infant or young child, is strongly suggestive of transposition, and a successful diagnosis has frequently been made on these features. In Thérémín's thirtieth observation this was based upon "cyanosis increasing when the infant cried, hypertrophy of the heart both in vertical and transverse diameter, the heart sounds loud and accentuated but pure, the aortic and pulmonary sounds distinct." In Ramm's case, aged fifty-six days, a probable diagnosis was made. Here also there was cyanosis from birth, no murmur, no accentuation or reduplication of the heart sounds, but dulness extending beyond the right sternal border and upward to the second rib, of so marked a character that a mediastinal tumor was at first suspected. In Thérémín's thirtieth, thirty-first, thirty-eight, and thirty-ninth observations the heart sounds were free from murmurs, although muffled, and cardiac dulness was increased to the right. On the other hand, a loud systolic murmur with maximum intensity at the apex was heard in Kelley's case, the same at the base and at the back in Pye-Smith's, and was probably produced by the patent foramen ovale present.

The patent ductus, patent foramen, or septal defect present, may produce their characteristic physical signs, and thus obscure the negative character of the auscultatory phenomena, which is significant of the clinical picture of an uncomplicated transposition.

Prognosis.—The duration of life varies in the three groups distinguished. In complete transposition it is usually very short. In 32 of the 40 cases in our series it varied between eleven months and a few days. When a septal defect is present, life may be considerably prolonged; the age of

¹ *Virchows Arch.*, 1863, lxxxii, 405.

sixteen years was attained by Keith's patient, eleven by Emanuel's, and four by Buchanan's. In partial or corrected transposition on the other hand, early adult life is usually reached. Birmingham's patient was twenty, Tonnie's twenty-one, Elliott's¹ nineteen, Young's thirty-six, and Geipel's forty-six years. Vierordt gives the following analysis of the duration of life in 75 cases. To this is added that of the 70 in our series, of which there were 57 classified as the primary lesion, and 13 complicating other defects.

DURATION OF LIFE IN TRANSPOSITION

Age.	Cases in this series.			Total.	Vierordt's cases.
	Complete	Partial.	Corrected.		
Born dead	0	0	0	0	3
1 to 24 hours	0	0	0	0	1
1 to 7 days	0	0	0	0	7
7 to 14 "	7	2	0	9	5
14 to 30 "	3	2	0	5	7
1 to 2 months	8	0	0	8	14
2 to 6 "	7	2	2	11	12
6 to 12 "	7	1	0	8	9
1 to 2 years	1	2	0	3	2
2 to 5 "	6	0	0	6	6
5 to 10 "	1	2	0	3	0
10 to 11 "	1	1	0	2	3
11 to 21 "	1	6	0	7	0
21 to 30 "	1	0	0	1	5
30 to 40 "	0	2	2	4	1
40 to 50 "	0	0	1	1	0
Age unmentioned	0	2	0	2	0
Total	43	22	5	70	75

PULMONARY STENOSIS AND ATRESIA.

Pulmonary stenosis is the form of cardiac defect most familiar to the practitioner. It is of much clinical importance on account of its comparative frequency, the relatively long duration of life, and the prominence of the cyanosis nearly always associated. To the student also it is a subject of the highest interest, for in its symptomatology and pathogenesis are focused the most difficult problems of congenital cardiac disease.

Owing to the wide variations in the conditions presented and the differing aspects from which the subject must be approached, a classification of the different forms is as difficult as it is necessary. Rauchfuss points out that the simple anatomical findings furnish the best guide to a useful grouping. Thus, the *degree of narrowing* is important, and a simple stenosis is to be distinguished from a complete atresia; from the stand-point of pathogenesis, the *seat and character of the stenosis* are criteria of much value; and thirdly, the *presence or absence of defects of the interventricular septum* provides a dividing line of the greatest importance. This last is important etiologically as indicating the stage of embryonic or fetal life at which the stenosis took place, and clinically in that the duration of life and symptomatology differ somewhat in the two groups.

¹ *Jour. Anat. and Physiol.*, 1877, xi, 302.

Statistics.—Pulmonary stenosis is probably the commonest of all cardiac anomalies. The cases are scattered so freely through the literature that an exact statistical statement is impossible. Vierordt estimated at least 300 in 1898, and placed coarctation of the aorta next in frequency with 130 cases. Among 181 anomalies of the heart which he analyzed, Peacock found 119 of pulmonary defect. In 1906 Keith¹ examined 185 specimens of cardiac malformations in the hospital museums of London, and found that in 135, or 70 per cent., there was an anomalous condition of the pulmonary tract, the deformity being in the conus of the right ventricle in 133 cases and in the pulmonary valve in 22. In his later communication,² among 272 malformed hearts examined in the various London Museums, Keith found 141 in which the defect was due to an imperfect transformation of the bulbus cordis of the embryo. Of these 141, in 19, there was incomplete fusion of the infundibulum with the body of the right ventricle (conus a separate chamber); in 44, partial arrest in development of the infundibulum; in 37, complete arrest of the infundibulum; in 23 fusion of semilunar valves; in 7, partial or complete absence of the body of the right ventricle with development of the infundibulum; in 4 subaortic stenosis; and in 7, congenital aortic stenosis.

Among the cases of anomalies analyzed here, there are 150 of congenital pulmonary disease. The proportion of stenosis to atresia in recorded cases analyzed is as follows:

	Stenosis.	Atresia.	Number analyzed.
Kussmaul	64	26	90
Rauchfuss	81	33	114
Peacock	90	29	119
Vierordt	83	24	107
Thérémín	20	10	30
This series	116	34	150

The relatively high percentage of atresia in Thérémín's cases is explained by the fact that his material was entirely among infants, in whom the mortality from atresia is high.

The condition of the fetal passages was the subject of statistical study by Meyer, Kussmaul, Taruffi, and other authors, of whose work a full review is given by Vierordt. A defect of the interventricular septum exists in the great majority. The number of cases with closed septum is relatively larger in atresia than in stenosis; thus Rauchfuss finds among 192 cases, 171 in which the interventricular septum is defective and 21 in which it is closed. Of these 21, 10 are cases of atresia and 11 of stenosis. Among Vierordt's 83 cases of stenosis are 71 with defective and 12 with closed interventricular septum; among his 24 of atresia, in 14 the septum was defective and in 10 it was closed. When the interventricular septum is entire, the foramen ovale is usually widely patent, but it also may in rare cases be closed.

Among the 116 cases of stenosis analyzed here the interventricular septum was defective in 95, and entire in 21 cases. In 12 of these 21

¹ *Festschrift, Quatercentenary Aberdeen University*, July, 1906.

² *Hunterian Lectures, Lancet*, 1909, ii, 359, 433, 519.

the foramen ovale was patent, but in 9 the auricular septum was also closed, and no communication existed between the two sides of the heart. Among the 34 cases of atresia the interventricular septum was defective in 26 and entire in 8 cases. Of these 8, in one the foramen ovale was also closed but there was a large patent ductus. The ductus arteriosus is nearly always patent in atresia but is usually closed in stenosis. Among the 82 cases of pulmonary stenosis classed as the primary lesion in the chart, the ductus was patent in only 11; of the 24 cases of atresia, it was patent in 15 cases. The condition of the cardiac septa and ductus in these cases was as follows:

	Stenosis.		Atresia.	
	Number analyzed.	Number with patent D. A.	Number analyzed.	Number with patent D. A.
F. O. and V. S. closed	7	0	1	1
F. O. patent, V. S. closed	11	1	5	4
F. O. closed, defect V. S.	40	5	7	3
F. O. patent, defect V. S.	24	5	11	7
Total	82	11	24	15

Rechtslage of the aorta is present in the majority of cases with septal defect, and is especially frequent in atresia. Among the 64 cases of pulmonary stenosis with septal defect, classified in the chart as the primary lesion, it was present in 39 cases, in 29 of which the aorta arose from both ventricles above the defect, and in 10 chiefly or entirely from the right ventricle. Among the 18 cases of atresia with septal defect the aorta arose from both ventricles above the defect in 5, entirely from the right ventricle in 10.

Pathology.—Pulmonary Stenosis.—The narrowing may involve the whole pulmonary tract, or be localized to the valve, artery, or conus. Two distinct types may be recognized:

1. In a few cases the stenosis is valvular in character and is produced by a thickening, shortening, or fusion of the pulmonary cusps. A thick diaphragm with three raphe of fusion on its arterial surface is usually formed, which protrudes into the pulmonary artery in a funnel-shaped way and is perforated by a circular or triangular opening of varying size. The pulmonary artery is frequently dilated above, may be normal, or somewhat thin-walled. The conus below the valve shares in the hypertrophy of the right ventricle, but is otherwise normal; the interventricular septum is usually closed. There is every evidence to show that the stenosis has originated in an inflammatory process in later fetal life after the heart has been fully formed.

2. In the second and larger group, the cusps may or may not be thickened or fused, but the stenosis is due to a rudimentary condition, hypoplasia, or deformity of some part of the pulmonary tract. In these cases a defect of the interventricular septum is usually associated and a deviation to the right of the aorta, so that this arises from both ventricles above the defect, or chiefly from the right ventricle, communicating with the left through the defect. Such forms, which suggest a developmental origin, make up the great majority of cases of pulmonary stenosis, and the combination of these three conditions, pulmonary

stenosis, defect of the septum at the base, and *rechtslage* of the aorta, is probably the commonest of all cardiac anomalies.

In the majority of cases—in Keith's estimate 90 per cent.—the conus of the right ventricle is involved in the deformity. Two distinct types of conus stenosis may be distinguished. The whole infundibulum may be more or less constricted, its musculature thickened, and the endocardium opaque. In a case of this kind, reported by Cautley,¹ the pulmonary cusps were delicate and healthy above the stenosis, but both they and the artery were very small. Usually the valves are thickened, fused, or rudimentary, and they are often bicuspid. Sometimes a thin diaphragm with delicate raphe showing no sign of inflammatory change, is stretched across the pulmonary orifice, suggesting an incomplete division of the endocardial cushions. In these cases a defect of the septum is almost invariably present.

A second group of conus deformities is that in which a cavity, described by some of the older pathologists as a third ventricle, is cut off from the sinus of the right ventricle by a definite septum perforated by a small opening. There are 19 in this series, including one case of atresia. Keith describes and figures an illustration of this anomaly. The infundibulum is enormously dilated and communicates with the sinus by a small opening with thickened fibrous borders. The pulmonary cusps are large and competent, the artery dilated above, and there is a small defect of the interventricular septum. Another variation of this form of conus deformity is figured by Andrewes.² The conus is atrophied and is represented by a small cavity with thick muscular walls. It communicates with the sinus of the ventricle by an opening admitting a crow-quill one-quarter inch below the pulmonary cusps, which are small, bicuspid, and not thickened.

Hypertrophy and dilatation of the right ventricle and auricle are constant in pulmonary stenosis, and in the cases associated with defect of the septum at the base and *rechtslage* of the aorta. In these the hypertrophy is sometimes most marked in the wall of the sinus of the ventricle, indicating that it had been produced by the force needed to send the blood into the aorta through the defect, rather than by the obstruction in the pulmonary artery. The aorta is usually thick walled and of large caliber. In the developmental cases the pulmonary artery is usually narrow and thin-walled, resembling a vein in structure. When the stenosis is confined to the valve, the artery may be dilated.

Pulmonary Atresia.—All that has been said of the seat and character of the deformity in pulmonary stenosis applies equally to a complete atresia. In a small series of cases the point of obliteration is at the valve, the artery dilated above, the foramen ovale widely open, and the septum entire. In Weiss's³ case the seat of atresia was in the conus, which admitted only a pinhead or a fine straw, and was lined by thickened endocardium; just above this were two fairly large pulmonary cusps, and the artery itself was comparatively large. There was a small patent foramen ovale,

¹ *Edin. Med. Jour.*, 1902, xii, 257.

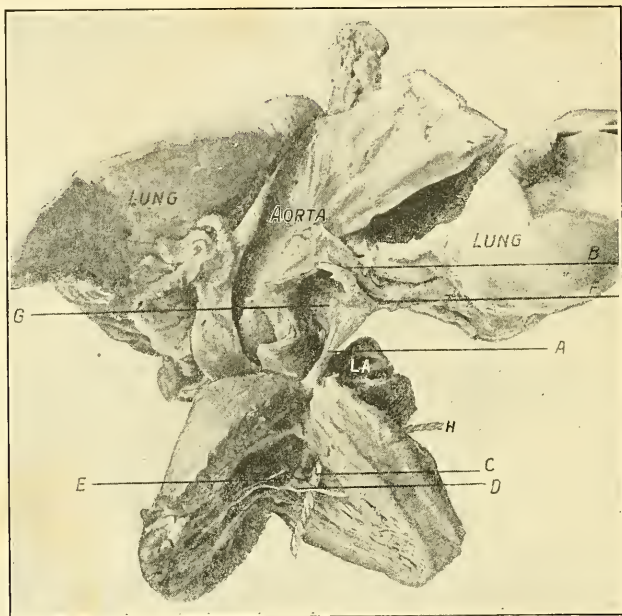
² *Trans. Path. Soc.*, 1865, xvii, 45.

³ *Brit. Med. Jour.*, 1877, ii, 378.

a large defect of the septum at the base, and a large thick-walled aorta arose from the right ventricle above the defect.

The pulmonary artery may be obliterated for some distance above the valve, forming a fibrous cord, which may emerge suddenly from the fleshy outer wall of the ventricle and give no sign of its origin from within, or it may be patent throughout, diminishing toward the orifice in a funnel-shaped way. In such cases the cusps may be seen thickened and fused with each other at the bottom of the cul-de-sac formed by the artery, or they may form a triradiate elevation of three fleshy cushions; or no trace of them may remain. The aorta is usually very large. When a defect in the septum is present it rides over it, or in many cases arises entirely from the right ventricle.

FIG. 36



Heart and lungs of an infant, cyanotic from birth, showing (A) atresia of the pulmonary artery; B, patent ductus arteriosus supplying lungs; C, defect of interventricular septum at pars membranacea, guarded by (D) an anomalous valve with false chordæ tendinæ; E, tricuspid orifice; F, left pulmonary artery; G, right pulmonary artery; H, cord passing through the septal defect; LA, left auricle. (From a specimen in the McGill Pathological Museum, presented by Sir William Osler.)

The foramen ovale is frequently widely patent. It may be the only means of communication between the two sides of the heart, the interventricular septum remaining entire. Such cases are less frequent, and the condition is more serious than that associated with septal defect.

The alterations in the cavities of the heart vary with the condition of the interventricular septum. When this is entire the left ventricle is greatly hypertrophied and dilated, and both auricles share in the enlargement, while the right ventricle undergoes a true concentric hypertrophy, its wall becoming greatly thickened and its cavity aplastic and

lined with opaque thickened endocardium, or in some instances completely obliterated. When a defect of the septum exists, the right ventricle is greatly hypertrophied and is dilated as well, and the right auricle is correspondingly enlarged, the left chambers remaining relatively small. When the aorta rides over the defect in the septum, the left ventricle may share in the hypertrophy.

The Pulmonary Circulation.—When the pulmonary artery is obliterated the blood supply usually reaches the lungs through the widely patent ductus, but this is sometimes closed or absent. Meckel first suggested that in these cases the dilated bronchial arteries might perform this function, and this is usually the case. The lungs were supplied from the left subclavian in Chambers' case, from a dilated ductus arising from the left subclavian in Ramsbotham's. In a case reported by Voss two large bronchial arteries passed into each lung, and were accompanied by an anomalous branch from each coronary. In Koller-Aeby's case the ductus was absent, and three large vessels, equalling the carotid in size, arose from the upper thoracic aorta at the site of origin of the bronchial arteries. The first turned to the right lung, following the bronchi; the others were given off as a common trunk, which divided into a larger branch going to the right and a smaller to the left lung.

Pathogenesis.—Two problems are presented. (1) Is the stenosis of inflammatory or of developmental origin? (2) What is the relation of the septal defect so often associated?

It must be recognized that a small group of cases occurs in which the stenosis is strictly limited to the valves and no septal defect is associated and which present appearances identical with those produced by the chronic valvular disease of postnatal life. Such cases must be supposed to be the result of an endocarditis in later fetal life.

In the large majority of cases a defect of the interventricular septum is associated, indicating that if the stenosis be due to an endocarditis, this must have occurred before the development of the heart was complete at the end of the second month of gestation. It is upon these cases that the discussion really turns. It is evident that if endocarditis can take place during the later stages of gestation, it may occur earlier as well. On the other hand, there are many cases in which the presence of associated defects and the absence of inflammatory action show positively that arrest of development has been the cause. The view is now generally held that in the past far too great weight has been laid upon the part which inflammatory processes take in the etiology of the many forms of pulmonary stenosis which date back to early embryonic life, before the development of the heart was completed. The theory of fetal endocarditis as a cause must now be considered to be of but limited application. The fault lies undoubtedly in most cases in a primary arrest of development.

Reference has been made to the explanation communicated by Keith, which is now generally accepted, that in the majority of cases the stenosis is primary in the conus, and is the result of an arrest of development at a stage when there existed in the heart a fourth primitive chamber, the bulbus cordis. In accordance with the researches of Greil, he de-

scribes three changes as taking place in the evolution of the mammalian from the primitive heart of the fish and reptilia: (1) The division of the primitive auricle and ventricle; (2) the submerging of the sinus venosus in the musculature of the right auricle; and (3) the separation of the bulbus cordis from the left ventricle and aorta, and its complete incorporation in the right ventricle as the infundibulum of that chamber. This last change takes place by an upgrowth of the ventricular musculature around the cavity of the bulbus, the musculature of the latter being replaced by that of the ventricle, in the same way as the musculature of the auricle replaces a great part of that of the sinus venosus. The author considers that "*the submergence of the bulbus constitutes a critical phase in the developmental metamorphosis of the heart, and it is during this time that malformations are apt to occur.*"

Four different types of conus stenosis are distinguished by him, of which the first is that well-differentiated form in which the conus forms a separate chamber, being separated from the sinus by a muscular partition. Peacock, in describing a similar case, compared it to the three-ventricled heart of the turtle, and considered that it represented an arrest of development. Keith explains the condition as being simply an arrest of development in which the infundibulum and body of the right ventricle have developed to a normal extent, while a constriction has remained between them, *representing the ventricular origin of the bulbus* or a persistence of the lower bulbar orifice. The other forms of conus stenosis, in which there is a constriction more or less complete of the whole infundibulum, he explains as an arrest of development of the bulbus as a whole, its musculature failing to become submerged in that of the right ventricle proper.

Associated Anomalies.—Grave cardiac defects are frequently associated, especially in pulmonary atresia, and constitute another argument in favor of a developmental origin. In Ettlinger's case there was a large defect in the interauricular septum above, with multiple defects of the interventricular septum, and the pulmonary veins opened into the right auricle. In Habershon's there was false dextrocardia, tricuspid stenosis, defect of the interventricular septum, and horseshoe kidney.

A fact of much importance is the presence of associated anomalies in cases of atresia with *closed* ventricular septum, which might reasonably be considered to be of inflammatory origin. It seems probable that the primary condition here was a narrowing of the conus or orifice in an arrest of development, and that the obliteration was produced by an endocarditis supervening in later fetal life.

Symptoms.—The majority of cases of pulmonary stenosis and atresia present the classical picture of congenital cyanosis in all its details. So frequent is the association between the two conditions, that *morbus cæruleus* and pulmonary stenosis have been considered almost synonymous terms. The clinical aspects vary to a certain extent with the presence or absence of defects of the interventricular septum, and with the degree of deformity. In stenosis with closed septum cyanosis is usually slighter and of later incidence, and the duration of life much longer. The most typical instances of congenital cyanosis with bluish discolora-

tion of the skin, becoming pronounced on exertion, clubbing of the fingers, dyspnœa, and cyanotic attacks are seen in the many cases in which pulmonary stenosis is combined with defect of the septum and *rechtslage* of the aorta. Pulmonary atresia differs from a simple stenosis in the more extreme degree of the cyanosis. These are the cases of true *morbus cæruleus*, in which a constant deep blue, or even purple, discoloration exists, increasing to black on violent exertion. Here the opposite condition in relation to septal defects is seen. When the septum is closed the cyanosis is more extreme and the duration of life correspondingly shorter. Pulmonary stenosis with defect of the septum in which no cyanosis is present is exceedingly rare, but a few cases are on record.

Physical Signs in Pulmonary Stenosis.—These are generally distinctive, but may be obscured by those of the septal defect so often associated. In typical cases, enlargement of cardiac dulness to the right and above, precordial bulging, epigastric and precordial pulsation indicate an enlargement of the right heart. Sometimes the cardiac impulse may be so violent that the head and neck share in the vibration of the chest. A thrill, localized to the second and third left spaces, or diffuse over the precordium, is fairly frequent. Its presence seems to depend somewhat upon the condition of the septa. Rolleston,¹ in reporting a case of stenosis with *rechtslage*, in which there was no precordial thrill, explains this by the presence of a large defect of the septum, through which the blood current passed with ease into the aorta. He says that the evidence in recorded cases is contradictory upon this point, and suggests a statistical study of it. A thrill was present in 17 of the 82 “primary” cases analyzed. In these the condition of the fetal passages was as follows:

Cardiac septa.	Number analyzed.	Number with thrill.
F. O. and V. S. closed	7	3
F. O. patent and V. S. closed	11	4
F. O. patent, defect V. S.	24	7
F. O. closed, defect V. S.	40	3

That is to say, in more than a third of the cases with closed ventricular septum a thrill was present, as also in 7 of the 24 in which both foramen ovale and ventricular septum were open. But in the 40 cases with closed foramen ovale and with defect of the septum a thrill was absent in all but 3; in one of which there was a large patent duct, which was apparently the cause.

These figures are puzzling at first, but interesting on reflection, and are large enough to be of value as facts. The inference is that a thrill is frequently present when the interventricular septum is entire, and also when a defect of that septum coexists with a widely patent foramen ovale; when the interauricular septum is closed and the interventricular open a thrill is rare, and when it does occur may perhaps be ascribed to the associated septal defect. Further statistics are needed.

The pulmonary second sound is weak or absent in a certain proportion of cases. Much stress has been laid upon the absence of pulmonary accentuation as a diagnostic sign of pulmonary stenosis, but in a number it has been distinctly louder than normal.

¹*Trans. Path. Soc., London, 1892, xliii, 32.*

A prolonged, harsh, rasping, or blowing systolic murmur heard over the whole cardia, but chiefly at the base, with its point of maximum intensity over the upper part of the sternum and the second left space, is present in the great majority of cases. It is transmitted upward toward the clavicle, along the course of the pulmonary artery, and over the sternum, but is faint or inaudible at the apex and to the right of the sternum. It may be so loud as to be heard over the whole chest. From this type important variations occur. (1) The murmur may be heard over the whole cardia, but with maximum intensity at the apex, as in Cassel's case, a boy aged thirteen years, with pulmonary stenosis and a patent foramen ovale, but the ventricular septum entire. In a case of Peacock's there was a loud systolic murmur over the whole heart and along the sternum, the maximum intensity of which was at the inner side of, and immediately above, the left nipple. In this instance a septal defect was associated. (2) In cases in which the septal defect is present the murmur may be heard over the *aortic* area and *along the carotids*. Eisenmenger mentions this as a diagnostic point for the association of pulmonary stenosis with a septal defect. In Scheele's¹ case, a girl aged fifteen years, with marked cyanosis, the pulmonary orifice admitted a thin pencil, the valves were small and shrunken, the conus was reduced to the size of a pea, and the septum was defective at the base. There was a systolic murmur along the course of the pulmonary artery and at the left sterno-clavicular articulation, which was transmitted far up the carotids and along both subclavians, and was most marked over the left carotid. It was heard also at the aortic cartilage. (3) The murmur may be heard in the back, in the left infrascapular region. This occurred in a number of the cases in this series, but in all a septal defect was associated, to which the transmitted murmur was probably due. (4) In a few cases physical signs are absent. Variot reports a child aged five years, with a large defect of the septum, and the pulmonary a small thin cord with rudimentary valves, who presented marked cyanosis with clubbing, but whose heart sounds were clear.

Diagnosis.—In the majority of cases the decided localization of murmur and thrill, the increased cardiac dullness to the right, the absence of pulmonary accentuation, and the presence of the distinctive symptoms of pronounced congenital cyanosis make a positive diagnosis possible. On the other hand, the variation in the character of the murmur and of the pulmonary second sound, and the occasional absence of cyanosis, render the diagnosis indefinite in a certain proportion of cases. That such atypical cases occur also makes it very difficult to exclude the possibility of pulmonary stenosis in the differential diagnosis of other cardiac defects. The presence of constant and marked cyanosis, the distinctive character of the murmur, and the fact that it is not usually heard in the back, are points in favor of stenosis. In patency of the duct, pulmonary accentuation is the rule, in pulmonary stenosis it is the exception.

Both the associated defect in the interventricular septum and the pulmonary stenosis have frequently been diagnosed. The presence of

¹ *Deut. med. Woch.*, 1888, xl, 294.

a thrill speaks rather for a closed septum, or for cases in which the foramen ovale also is patent. In a large number of cases the presence of the two distinctive murmurs can be easily traced, that due to the pulmonary obstruction heard best at the base and transmitted beneath the clavicle, that due to the defect localized at the fourth space, heard also in the back, both harsh, but of the two, the pulmonary usually of a more blowing character.

Course.—The duration of life in pulmonary stenosis with closed interventricular septum is relatively high. Peacock reports a patient dying at forty-five years, and the lowest age in this series was four years. The possibility exists in such cases that the stenosis had advanced, or even originated since birth. In stenosis with septal defect death occurs earlier, but adult life is also sometimes attained. The maximum age in this series was twenty years. In pulmonary atresia life is very short. The patients with closed septum all die within the first few months. When a defect of the interventricular septum exists these subjects may live some years. The highest age recorded was thirteen years, in one of Peacock's cases. The table gives the duration of life in the cases in the series in which this point is mentioned:

PULMONARY STENOSIS.

Age at death.	V. S. closed.	F. O. closed, defect V. S.	F. O. patent, defect V. S.
Before 1 year	0	4	3
1 to 7 years	2	17	8
7 to 14 years	4	6	5
14 to 20 years	5	8	5
20 to 28 years	6	3	1
28 to 45 years	1	0	0
	—	—	—
Number of cases analyzed	18	38	22

PULMONARY ATRESIA.

Age at death.	V. S. closed.	F. O. closed, defect V. S.	F. O. patent, defect V. S.
In first week	1	0	0
1 to 4 weeks	1	0	2
1 to 3 months	1	1	1
3 to 6 months	3	1	2
6 to 9 months	0	0	1
9 to 12 months	0	0	4
1 to 5 years	0	3	0
5 to 10 years	0	1	0
10 to 13 years	0	1	1
	—	—	—
Number of cases analyzed	6	7	11

Many patients who survive until early adult life die, not of the lesion, but of pulmonary tuberculosis. The frequency of this disease in pulmonary stenosis and its grave prognosis can be no longer disputed. The cause of the predisposition seems to be: (1) The reduced blood supply to the lungs produces an anemic condition which favors infection; (2) the marked cyanosis usually present depresses the general powers of resistance and tends to destructive tissue metabolism; (3) the subjects of pulmonary stenosis frequently live to an age when tuberculosis is

likely to invade the organism when the nutrition is low. This last point is illustrated in an interesting way in this series. Among the 18 patients with closed septum, in whom the duration of life was longer, pulmonary tuberculosis occurred 7 times. Among the remaining 64 patients with defect of the interventricular septum (in whom life was shorter) it occurred in only 9 cases, making an incidence of 16 cases in the 82.

Another not infrequent termination is by infection from an acute endocarditis developing at the seat of the defect. Robinson reports two instances in patients who both died at the age of twenty years, in both of whom the conus formed a separate chamber with narrow bulbar orifice. In the one case there were large vegetations on the conus wall, in the other these formed a fine fringe around its ventricular orifice, and coarse outgrowths about the associated defect in the interventricular septum. Acute endocarditis appears to be especially common in this form of conus deformity, and among the 19 cases in which the conus formed a separate chamber, recent vegetations fringing the conus orifice, on the wall, or on the tricuspid valve were present in 6. In Saundby's case there was a vegetative arteritis of the pulmonary artery, but none of the valves.

DILATATION OF THE PULMONARY ARTERY.

Dilatation of the pulmonary artery is very common in combination with certain cardiac anomalies but is rare as an isolated condition. A few cases are recorded in which it appears to be primary and to originate in an irregular division of the common arterial trunk. The main vessel is diffusely enlarged and its branches are tortuous and dilated, but the heart and lungs are otherwise normal. The artery is usually dilated in persistence of the fetal passages connecting the two sides of the heart, especially in patent ductus and defects of the lower part of the interauricular septum, or in widely patent foramen ovale. In the two latter conditions hypoplasia of the aorta is frequently associated and it is difficult to say which is the primary condition. The dilated artery may be atheromatous even in young subjects.

In defects of the interventricular septum at the base, the hypoplasia of the pulmonary artery so often present may give place to a marked dilatation. This was the case in 9 among the 34 primary defects of the septum in this series. The clinical manifestations of pulmonary dilatation are discussed by Abrahams¹ with the report of a case in which this was diagnosed as the primary condition.

CONGENITAL AORTIC STENOSIS OR ATRESIA.

Subaortic Stenosis.—This term has been applied to a curious annular thickening of the endocardium of the left ventricle, a few millimeters below the aortic valves, which involves the base of the aortic segment of the mitral valve, and encircles the ventricular wall at this point, and

¹ *Jour. Am. Med. Assn.*, 1913, lx, 1150.

leads in most of the cases, to a localized narrowing of the cavity. The cases recorded are not numerous (seven in all), but the condition, when present, usually leads to serious results, and is therefore important. The thickened ring of tissue is often the seat of a chronic inflammatory process, probably of later incidence, but there can be little doubt that it is itself of congenital origin. Microscopic examination of the ring in a case reported by Moore showed it to be non-inflammatory in character. Keith explains it as an arrest of development, analogous to the conus stenosis of the right ventricle, the bulbus failing to atrophy about the root of the aorta.

Endocarditis frequently develops both at the defect and at the aortic valves above it, and may lead to further contraction at these points. Shennan¹ and Smart² report two such cases under the term "double aortic stenosis," and a third is recently recorded by Thursfield and Scott.³ In the last, the aortic orifice was narrowed by a fibrous ring, situated on the interventricular septum, just below the undefended space and extending over the anterior mitral segment, and the aortic valves were thickened and fused; there was a thin line of fibrosis in the otherwise healthy aorta just above the margin of the valves, and slight coarctation at the isthmus. In Shennan's patient, and in that of Fletcher and Beattie, a thick calcareous ring lay below the thickened and ulcerated valves which were the seat of a malignant endocarditis.

Most of these patients reach adult life, and the clinical significance of the condition lies chiefly in the frequent incidence of acute endocarditis. The picture is that of an acquired aortic stenosis. Slight symptoms may exist from childhood, or no sign of the presence of the defect may be given until an acute endocarditis develops, or failing compensation sets in. The systolic murmur produced by the constriction may be very rough, and audible some distance from the chest wall. A precordial thrill existed in some cases.

Congenital Stenosis and Atresia of the Aortic Orifice.—Aortic stenosis of antenatal origin is not common and the duration of life with it is very short. Two forms may be distinguished; those apparently inflammatory, with the stenosis limited to the valves and the ventricular septum entire, and those apparently due to an arrest in development. Unlike pulmonary stenosis, the inflammatory forms are here the commoner, fetal endocarditis, although rare in the left heart, usually involving the aortic orifice. Thérémín collected 17 cases, in only 2 of which was there a defect of the septum. In our series there are 6 cases, 5 of which are inflammatory.

Mönckeberg⁴ reports a case of inflammatory origin in an infant of four days, and refers to 12 cases in the literature. He ascribes the occurrence of the fetal inflammation to probably the fifth month of gestation, for the left heart was very small, and the right side so hypertrophied that the apex of the right ventricle formed a recess-like cavity below the left, a condition typical of a heart in which the right ventricle had carried on the systemic circulation through the ductus arteriosus

¹ *Lancet*, 1905, vol. i, 21.

³ *Brit. Jour. Child. Dis.*, 1913, x, 104.

² *Ibid.*, 1904, vol. ii, 1417.

⁴ *Deut. path. Gesell.*, 1907, xi, 224.

for a long time. In aortic atresia the left ventricle is aplastic, and when a defect of the septum exists, may even be obliterated. The foramen ovale and ductus, are nearly always widely patent, the latter supplying the systemic circulation.

Cyanosis is usually slight or absent in cases of aortic stenosis, but marked in atresia. Physical signs may be absent, or there may be a loud systolic or double murmur heard over the whole chest. In both conditions the duration of life is very short. In aortic atresia the highest age attained was twenty-seven weeks. Simmons¹ described an interesting case in an infant aged sixteen weeks, cyanotic from birth, with widely patent foramen ovale and ductus arteriosus, the left ventricle aplastic, the right ventricle greatly hypertrophied, and the aortic cusps fused to form a cone.

Left-sided Conus Stenosis.—Schmincke² describes two cases in adults of a peculiar muscular stenosis of the conus of the left ventricle, with healthy aortic valves, and no apparent cause, which he thought must be of congenital origin, due to a primary asymmetry in the formation of the left ventricle.

ANOMALIES OF THE SEMILUNAR CUSPS.

These cusps may be increased or diminished in number and defective, fenestrated, or otherwise malformed. A row of supplementary cusps may exist or they may be the seat of attachment of anomalous bands.

Increase in Number.—Supernumerary cusps sometimes occur in the pulmonary artery and, less frequently in the aorta. A more or less perfectly formed fourth cusp of varying size, but frequently smaller than normal, may be inserted between two of the others. Or the usual number of segments may exist, and the sinus behind one of these be divided by a raphe which runs from the back of the cusp to the aorta, indicating fusion of the additional segment or imperfect division from its fellows. In rare instances five cusps occur. Peacock figures a case of five aortic cusps, and Dilg enumerates from the literature 4 cases, in 2 of which the five cusps were in the aorta, and in the pulmonary artery.

The supernumerary cusps have sometimes been explained as an effort at repair of some inflammatory process of long standing, but when the fourth segment is perfectly formed, or the raphe indicating it shows no sign of thickening (as in a case in the McGill Museum), a true malformation must be concluded, which is usually explained as a formation by excess. As this condition is of congenital origin, the cusps are generally so adapted to each other as to be competent to close the orifice, no insufficiency resulting; they occur usually in a heart free from other malformations, and are of very infrequent occurrence. Their clinical significance is slight, and lies chiefly in their tendency, like all valvular anomalies, to become the seat of endocarditis.

Diminution in Number.—A bicuspid pulmonary valve is not uncommon with other cardiac anomalies, especially transposition and septal defects. A bicuspid aortic valve usually occurs in an otherwise normal heart or

¹ *Intercol. Jour. of Austral.*, February 20, 1906.

² *Deutsch. med. Wchnschr.*, 1907, xxxiii, 2082.

associated with coarctation or hypoplasia of the aorta. In some instances both pulmonary and aortic valves may be bicuspid. The anomalous segments may be large, with smooth surfaces, showing no sign of further division, a true reduction in number existing; or one or both may present on the arterial aspect a ridge or raphe imperfectly dividing the sinus behind it into two parts, and indicating either a fusion of two formerly independent segments or a beginning separation of a single cusp into two elements; in other instances a single membranous ring or diaphragm may exist with two such raphes on its aortic surface, indicating the union with each other of all three cusps. Where such a raphe is absent, the condition is undoubtedly a true malformation, but where this exists, the origin of the bicuspid state of the valve admits of much discussion. Peacock arrived at the conclusion that the majority of cases were congenital, due either to an original malformation or to fusion in a fetal endocarditis.

A series of cases illustrating the same line of thought was published by Osler.¹ As pointing to a fusion originating in fetal life, he enumerates (1) the presence of a low, sometimes half obliterated, raphe behind one of the cusps; (2) compensatory changes in the fused cusps, so that their free edge becomes equal to or even shorter than the single segment; and (3) the fusion of the coronary or right and left segments of the valve. That the lateral (right and left) segments are the seat of the congenital fusion, the posterior cusp remaining always single, is stated also by Birch-Hirschfeld.

Thickening of cusp and raphe does not prove that the fusion is not of congenital origin, for endocarditis is likely to supervene on any valvular anomaly. On the other hand, it is admitted that many cases are of postnatal inflammatory origin. Such postnatal fusion may be reasonably deduced when (1) the two sections of the cusp are approximately equal; (2) when the raphe dividing them has its superior origin on a level with the superior origin of the unaffected cusp (instead of at the lower level, as described by Osler); and (3) *when in addition the only thickening observable is in the angle between the fused cusps*. This latter point has been called to the attention of the writer by Dr. Adami, who points out that the free part of the cusps, being in constant motion, is but little liable to undergo inflammatory adhesion, and that this will be prone to occur at the point of their insertion into the orifice wall, which is the only portion of their edge that is fixed and relatively motionless. Therefore, inflammation originating at the angle of junction of contiguous cusps may lead to localized obliteration of the primary angle, or to fusion of the cusps with a new immovable angle of junction further removed from the aortic wall, a progressive fusion occurring.

When a thin delicate raphe exists behind one of the segments of a bicuspid valve without any trace of thickening, Babes insists that it cannot be ascribed to a fusion in fetal endocarditis, but must be regarded as a true malformation dependent perhaps on incomplete division of an originally single cusp. The semilunar cusps originate from the four distal

¹ *Montreal General Hosp. Reports*, 1880.

bulbar endocardial ridges, two of which are divided by the descent of the aortic septum, so that a third segment is placed in each artery. The four cusps of the undivided truncus are sometimes seen in the cases of common arterial trunk.

The results upon the heart and circulation of a reduction in the number of the aortic cusps may be summed up as follows:

1. The segments may approximate and be perfectly competent, no pathological effects ensuing. This is proved by the occasional finding of a bicuspid valve in healthy adults even of advanced age.

2. The gradual bulging of the cusps, their greater length, the free space that sometimes exists between them, perhaps a yielding of the aortic ring, lead frequently to a valvular insufficiency or to a narrowing of the orifice.

3. Endocarditis commonly supervenes, either as the acute, often malignant form, or as a chronic inflammatory process, leading to thickening and deformity of the cusps and to subsequent valvular disease.

4. Atheromatous changes at the base of the aorta have been frequently noted, and in 6 of the 11 cases described by Babes and Deteindre there was an aneurismal bulging of the right posterior wall of the aorta, which formed in 5 instances a definite aneurism, from the rupture of which, in 2 cases, death ensued. This is seen also in two cases in the McGill Museum.

This remarkable combination of an aneurism of the base of the aorta with a bicuspid valve is believed by Babes to be directly connected with the bicuspid character of the aortic cusp below it, and is ascribed by him (*a*) to an extension of the same thinning or trophic process that led to the anomalous condition of the cusp, (*b*) to the lack of support given to the aorta at this its weakest point, and (*c*) to the frequent insufficiency of the cusps and the yielding of the aortic ring.

Miscellaneous Anomalies.—Dilg reports a remarkable case, in a child aged two years, of an endocardial fold divided roughly into two cusps with their convexity toward the ventricle, just below the base of a bicuspid aortic valve, both coronaries being behind one cusp. Banks¹ reported a woman, aged thirty-four years, with physical signs of aortic insufficiency and a loud, musical murmur at the base, audible at some distance from the chest, whose heart was hypertrophied and presented a cribriform condition of the aortic valve, and one-quarter inch below it in the left ventricle three other rudimentary cusps. These may be of compensatory, postnatal origin, as in a number of other cases recorded of long-standing aortic insufficiency.

In a case in the McGill Museum, reported by Campbell and Hepburn,² of pulmonary conus stenosis with septal defect, two well-formed valves are situated 1.8 cm. behind the pulmonary semilunar cusps, at the point which marks the lower bulbar orifice, and the site of the proximal bulbar swelling in the embryo. This is an entirely unique finding and suggests an atavistic reversion to the cusps seen at this point in the dipnoan heart.

In one of Babes' cases of bicuspid aortic valves, a peculiar band, like

¹ *Dublin Hosp. Gazette*, 1857, p. 330.

² *Can. Med. Assn. Jour.*, 1913, iii, 871.

a papillary muscle of the mitral valve, traversed the sinus of Valsalva. Hektoen¹ quotes from the literature several other instances of anomalous cords at the level of the valves, and a case observed by himself of a large defect at the base of one of the segments, all of which he ascribed to defects in the development of the aortic septum.

Defective Development of the Semilunar Cusps.—In a few instances of bicuspid valve a gap may be left on the wall of the vessel between the segments where evidently no third cusp has formed. This occurred in two of Deteindre's series. A remarkable instance of such a defect in the pulmonary valve is recorded by Stinzing. Here there are only two pulmonary cusps, and a large free space occupying the position of the third was traversed by two low ridges, evidently its rudiments. The heart was from a woman, aged sixty-four years, presenting signs and symptoms of pulmonary insufficiency, a history of pneumonia eight months before death, and failing compensation since.

PRIMARY DEFECTS OF THE AURICULOVENTRICULAR ORIFICES.

Congenital disease of the auriculoventricular valves differs from that of postnatal life chiefly in its infrequency, in the more extreme character of the process, atresia being more common than stenosis, and in the fact that the right side of the heart is usually affected rather than the left. Owing to the rarity of the cases, to the short duration of life, and to the fact that in the infant heart the picture presented is hard to distinguish from that of the more frequent lesions at the arterial ostia, this subject is not of great clinical importance, and its chief interest lies in the contribution which it brings to our information upon the question of the pathogenesis of cardiac defects.

Tricuspid Stenosis.—Although this lesion is not very uncommon in adults the cases which can be proved to have originated in intrauterine life are very rare. Vierordt knew of only three instances, unassociated with disease of the pulmonary valves, in the literature. In combination with pulmonary stenosis or atresia it is more frequent. A good illustration of the latter combination is seen in a specimen in the McGill Museum, presented by Sir William Osler. In the heart of a cyanotic infant aged four months, both pulmonary and tricuspid valves are thickened, shortened, and fused, and their orifices markedly reduced; the ventricular septum is entire, the foramen ovale widely patent, the right auricle hugely dilated, and the tricuspid surmounted by recent vegetations. Such cases are undoubtedly of inflammatory origin, and are of value as proving that fetal endocarditis, although it has been overrated as a cause, certainly has its place as an etiological factor in congenital cardiac disease.

Tricuspid Atresia.—Although in itself rare, tricuspid atresia is the commonest of all congenital lesions of the auriculoventricular cusps. Rauchfuss collected 16 cases from the literature of which 5 were due to a defect in development, 5 were apparently inflammatory, and the remainder were of "doubtful" origin. Since then additional cases have

¹ *Chicago Path. Soc.*, 1905.

been reported by Chapotot (quoted by Vierordt), Sieveking, Kühne¹ (two cases) Bernstein² and Wieland.³

Pathological Anatomy and Pathogenesis.—Cases of inflammatory origin must be distinguished from those due to a defect in development, for the latter present several points of special interest. Those of inflammatory origin have usually progressed through a stenosis and show distinct evidence of an antenatal valvulitis in the form of an extensive cicatricial contraction of the endocardium adjacent to the obliterated tricuspid orifice, and often of the pulmonary valves. The developmental cases, on the other hand, may present no sign of inflammation, but the tricuspid orifice is absent, and either shows no trace of its presence, or this is marked by a shallow groove, the tricuspid segments are lacking, and the right auricle is divided from the right ventricle by a thick muscular septum. Kühne, and subsequently Wieland, subdivided these developmental cases into a group of (a) “isolated” primary atresias in which certain pathological changes of a secondary nature are constant so that a definite type is set up, and (b) tricuspid atresia complicated by other grave cardiac anomalies of independent origin, such as transposition of the arterial trunks, pulmonary atresia, etc. Eight cases of the “isolated” form that constitutes the first group were separated by Kühne, and later by Wieland, from the others. To these may be added one by Bernstein from our series. The changes in all of these are practically identical and clearly indicate the sequence of events. There is an entire absence of the tricuspid orifice, and the body of the right ventricle is an aplastic structure, while the left is highly hypertrophied and dilated, appearing at first sight to form the whole heart, with the right chamber as an appendage to it; the right auricle is also hugely dilated and the foramen ovale is widely patent, or a defect of the interventricular septum exists; in addition there is always a defect in the muscular interventricular septum leading from the cavity of the left ventricle into the dilated conus of the right ventricle and thence into the pulmonary artery. The course of the circulation is necessarily from right to left auricle through the foramen ovale, and thence to the left ventricle, from which the blood is distributed in part to the aorta and in part through the septal defect to the pulmonary artery. The aorta is usually dilated, and the pulmonary is normal or somewhat reduced in size owing to the smallness of the chamber from which it springs.

These cases of “isolated primary tricuspid atresia” are of interest from the standpoint of the pathogenesis of ventricular septal defects, for they show that the old mechanical or congestive theory of septal defects in pulmonary stenosis, in which the defect was thought to be secondary to the raised pressure in the right ventricle, which has long been justly discarded in this connection, at least in regard to the developmental forms of pulmonary stenosis, must be accredited here. That is to say, the septal defect in tricuspid atresia is here evidently secondary to the congestion in the left ventricle which forces an outlet in the conus

¹ *Jahrb. f. Kinderh.*, 1906, lxiii, 235.

² *New York Path. Soc. Reports*, February, 1906.

³ *Jahrb. f. Kinderh.*, 1914, lxxix, 320.

of the pulmonary artery and this allows the circulation to be maintained. Wieland points out and insists on the importance of Kühne's separation of this group, with its constant secondary complex, on this account.

It should be remembered that cases of developmental tricuspid atresia with or without complicating cardiac anomalies, constitute one well recognized form of the *cor biatriatum triloculare*. The subject is discussed under that head.

Etiology.—The causation of the cases of inflammatory origin is that of fetal endocarditis elsewhere. In tricuspid atresia the secondary ventricular septal defect is bound to occur, for the proper maintenance of the circulation as well here as in the developmental forms.

Much interest attaches to the causation of the developmental forms of tricuspid atresia. In the embryo the auricular canal opens at first by a common orifice into the left side of the common ventricle, and later by a process of shifting to the right comes to lie more in the median line. The theory had been advanced that either a lack or an exaggeration of this shifting to the right would lead to a wrong adjustment of the parts, and to a mitral or tricuspid atresia. Again, the auriculoventricular orifice is divided into the mitral and tricuspid ostia by the growth of endocardial cushions in its centre, and by a union of these with the interauricular and interventricular septa. Should these cushions become deviated to the right or to the left in their formation they may become adherent to the corresponding wall of the common ostium and thus lead to tricuspid or mitral atresia. Rokitsansky thus explains his case of mitral atresia. In that by Robertson the tricuspid atresia present was ascribed to a fusion of the endocardial cushions with the malposed auricular secondary septum, in consequence of a persistence of the *valvulae venosæ* which formed a coarse network across the cavity of the right auricle. The suggestion has also been made that a premature obliteration of the ductus arteriosus during early fetal life, might lead to aplasia of the right ventricle and tricuspid orifice by cutting this part of the heart out of the fetal circulation. This possibility is disproved, however, by the fact that in several of the cases this passage is freely patent. The conclusion remains that the probable causation of mitral and tricuspid atresia lies in the mal-position and irregular union of those parts of the cardiac septa dividing the mitral from the tricuspid ostium.

Symptoms and Signs of Tricuspid Stenosis not Atresia.—Cyanosis may be present from birth, or may develop after a few days or weeks. In the classical developmental type described above it is usually extreme in the end, though its onset may be delayed for some time. In Bernstein's case, aged two years and eight months, it did not appear until the sixteenth month, but then became marked with clubbing, and a polycythemia of 10,000,000 developed. This late appearance was possibly explained by the absence in this case of the auricular septum, a condition which must have facilitated the circulation. On the other hand, Kelley's patient, a delicate, unhealthy child, showed only slight lividity on crying or when he had a cold, and in Sieveking's case, dying at nine weeks, cyanosis was absent throughout, but dyspnoea was a prominent symptom.

Dyspnœic attacks are a prominent feature, are often of daily occurrence and are frequently the direct cause of death.

Physical signs are not very characteristic, being obscured by those of the septal defect that in tricuspid atresia is always present, and by the fact that a systolic murmur with maximum intensity over the right ventricle, such as is usually produced in these cases, may with difficulty, be distinguished from one generated at the pulmonary area. The marked hypertrophy of the left combined with the smallness of the right ventricle is of assistance in the differential diagnosis from pulmonary valve disease, although allowance must be made for the increased cardiac area produced by dilatation of the right auricle. This feature was indicated in Wieland's patient by a zone of dulness to the right of the vertebral column behind. His case was characterized also by a strong systolic murmur and precordial thrill of maximum intensity at the apex, both of which were of a *curiously intermittent character*.

Duration of Life.—Very few of the developmental cases of tricuspid atresia live more than one year. Bernstein's patient reached two years and eight months, a relatively high age that is perhaps explained by the almost complete absence of the interauricular septum that was present. In the inflammatory cases, in which the atresia has probably progressed through a stenosis, adult life is frequently attained. Such was Bierdach's case dying at twenty-eight years.

Congenital Mitral Stenosis.—This is even rarer than the same lesion at the tricuspid orifice. A typical case evidently due to an antenatal valvulitis, in a child of ten months, with cyanosis and dyspnœa from birth, is reported by Simmons. A curious combination of dwarfism and mitral stenosis in patients who have attained adult life has been observed. L'Abbe reports a case in a woman, aged twenty-seven years, of extremely small stature (1 meter high, 43 kilos weight), puerile intelligence, and marked infantilism. There was a clear history as well as physical evidence of congenital syphilis, and a pure mitral stenosis.

Mitral Atresia.—A complete obliteration of the mitral orifice is still rarer than stenosis. The same remarks apply in regard to etiology as in tricuspid atresia, but here a primary defect in development may be almost constantly assumed. Grave associated anomalies are also nearly always present, and give additional proof of a teratological origin. In Thérémín's observation of an infant aged two days, the left auricle and ventricle were aplastic without any trace in the latter of a mitral orifice, its walls being formed throughout of finely reticulated muscle fibres; the foramen ovale was closed, the interventricular septum defective, the pulmonary valve bicuspid, and the aorta appeared to arise from the right ventricle; there was a *horseshoe kidney and double ureter*. Lawrence and Nabarro give a similar case of mitral atresia, defect of the septum, aplastic left ventricle, the aorta arising behind the pulmonary artery from the right ventricle, with *coarctation of the aorta, transposition of the stomach, absence of spleen and hepatic section of inferior vena cava; anomalies in form of liver and lungs*. In Rokitansky's case of aortic and mitral atresia with defect of the septum, patent foramen ovale,

and dilated pulmonary artery, in a child aged twelve days, there was an *accessory right bronchus*.

Congenital Mitral and Tricuspid Insufficiency.—These lesions may result from a primary malformation of the cusps or from secondary deformity in the arrest of development of neighboring structures, as in persistent ostium primum. Or they may be due to thickening and shortening of the valve in a fetal endocarditis; thus Barth and Roger describe a case in which, on auscultation before birth, a long, loud, rough murmur was heard accompanying the heart sounds. The child was stillborn three days later, and the right ventricle was found dilated, the tricuspid orifice enlarged, and its cusps shrunken and insufficient, and evidently the seat of an endocarditis. In the case of Steffen, of a child aged ten and a half months, there were no tricuspid segments, but the valve formed a low ridge which was thickened, reddened, and slightly jagged. The mitral cusps were similarly thickened and reddened, and one of them was reduced likewise to a narrow ridge.

Congenital Mitral Insufficiency.—Steffen's case is the only instance of congenital mitral insufficiency found in the literature. True congenital tricuspid insufficiency is also rare, probably there are not a dozen cases.

ANOMALIES OF THE AURICULOVENTRICULAR CUSPS.

Double Auriculoventricular Orifice.—A second valvular opening supplied with its own cusps, chordæ tendineæ and papillary muscles, may lie within the segments of an otherwise normal auriculoventricular valve. Seven such cases are recorded, six of double mitral orifice by Greenfield,¹ Cohn,² Degen,³ Stuhlenweisenberg,⁴ and Camisa,⁵ and one of double tricuspid by Piseni.⁶ In Stuhlenweisenberg's case, and in one of Camisa's, the two orifices were of equal size, and were separated by a bridge of valve tissue which supplied a cusp to either opening; in all the other cases the second opening was much smaller, and lay in one of the segments of the primary orifice.

Two hitherto unpublished cases of the latter description, are in the collections of the Harvard and the McGill Medical Museums. In the Harvard case, an opening 2 cm. long lies in the aortic cusp of the main mitral orifice, and leads into an aneurismal pouch formed by the apex of this segment, which communicates with the cavity of the ventricle by numerous fenestrations. The McGill heart (Fig. 37) is of bizarre external form owing to its bifid apex, deep auriculoventricular groove, and hypertrophied right chambers. The interauricular septum presents a small valvular patent foramen ovale above, and is absent in its lower two-thirds, a large crescentic defect (*persistent ostium primum*) existing. The mitral valve is replaced by a single large segment which is cleft in its anterior portion, passing forward from either side to be inserted

¹ *Trans. Path. Soc.*, 1876, xxvii, 128 (with plate).

² *Inaug. Dissertation*, Königsberg, 1896 (with plate).

³ *Inaug. Dissertation*, Greifswald, 1903.

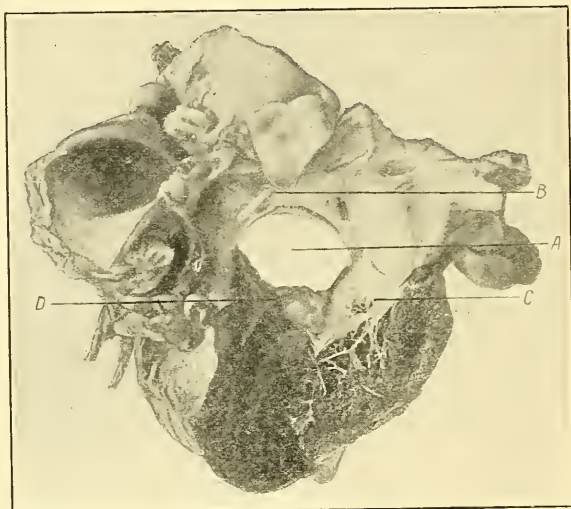
⁴ *Centrab. f. Pathol.*, 1912, xxiii, 1027.

⁵ *Ibid.*, p. 342

⁶ *Di una rarissima Anomalia della tricuspid*, Perugia, 1888.

into the middle of the base of the interventricular septum where this bounds the interauricular defect below. The secondary mitral ostium lies in the posterior half of this large primary segment, 7 mm. back from its free margin. It is a perfect valvular opening admitting a lead-pencil with two well-formed cusps attached to slender chordæ, arising from two short papillary muscles which lie behind and independent of the single group from which the chordæ of the primary segment spring. The right auriculoventricular valve is malformed and an irregular excavation in its septal cusp suggests an unsuccessful attempt at a double tricuspid ostium. The aortic valve is bicuspid. The endocardium is healthy.

FIG. 37



Heart of a child, aged five years, showing; *A*, defect of lower part of interauricular septum; *B*, patent foramen ovale; *C*, double mitral orifice; *D*, cleavage of mitral segment. (From a specimen in the Pathological Museum, McGill University.)

Etiology.—Camisa believed a fetal endocarditis had led to a fusion of segments at their apices and to the formation of secondary orifices. Cohn and Stuhlenweisenberg suggest a malformation by excess, a view supported in the latter's case by the equal size of the two orifices. Pisenti supposed a fenestration of the endocardial cushions, which had transmitted the blood stream in early embryonic life and had become transformed into a second valvular orifice by a natural adaptation of growth, the papillary muscles and chordæ growing up to its borders.

In the two specimens seen by us, Pisenti's explanation seems to apply, the marked irregularities in both auriculoventricular valves due to the auricular septal defect in the McGill specimen, and the multiple fenestrations in the Harvard case, alike arguing for such accidental origin at an early embryonic period. Camisa's theory of a fetal endocarditis is not tenable in the case of the McGill specimen and others in which the endocardium is free from every trace of sclerotic change.

Symptoms.—The double orifice is in itself of no clinical significance, the secondary segments functioning as normal valves. In the majority of the cases, including Cohn's patient, who died at seventy-one years, both sets of valves were thin, healthy and competent. Chronic endocarditis had supervened in both Camisa's cases and in Stuhlenweisenberg's. In the latter a loud systolic murmur over the precordium was associated with insufficiency and sclerosis of the segments of the *anterior* mitral ostium, the posterior remaining free.

Displaced Orifice.—A double mitral orifice is described by Andrewes,¹ in which two orifices separated by a fibrous septum lay one behind the other in the left ventricle. The right ventricle was rudimentary, the interventricular septum defective and the tricuspid valve absent. A deflection of the septum to the right so that both orifices are placed in the same ventricle was assumed.

Miscellaneous Anomalies.—Various minor defects, as irregularly formed or accessory leaflets and anomalous arrangement of the chordæ tendineæ or papillary muscles occasionally occur, and may in some instances contribute to an insufficiency of the valves.

PRIMARY PATENCY AND ANOMALIES OF THE DUCTUS ARTERIOSUS BOTALLI.

The ductus arteriosus of the fetus is a short, thick trunk, 10 to 15 mm. long, running from the left branch of the pulmonary artery directly after the bifurcation to the under side of the arch of the aorta just beyond the origin of the left subclavian artery, which serves to carry the unaërated blood, returned from the head and upper extremities, to the descending aorta, whence it passes to the placenta. At birth the ductus undergoes a rapid involution, its lumen becomes practically impermeable about the third week of life, the alterations in its wall, which lead to its permanent obliteration, going on for some months, and finally transforming it into the *ligamentum arteriosum* of later life. The average diameter of the patent ductus at birth is given by Vierordt at 5 to 6.8 mm. and by Thérémín as 4.8 mm. But when filled with fluid during life, or experimentally injected directly after death, it is found to be much larger. Thus in a series of infant hearts prepared by Klotz, in which he injected the ductus from the aorta with gelatin at autopsy, it was found in the newly born to be fully equal in size to the main pulmonary trunk. He ascribes its apparent smallness as usually seen postmortem to the firm contraction of the muscular wall.

The ductus may (1) remain patent throughout life, (2) undergo aneurismal dilatation, (3) it may be absent, or (4) it may have an anomalous origin or course.

Patency of the ductus is not infrequent in combination with other cardiac defects, especially those in which there is some serious interference with the pulmonary circulation. It occurred in 166 of this series of cases, in 21 of which it was combined with pulmonary atresia,

¹ *Trans. Path. Soc.*, London, 1903, liv.

in 14 with pulmonary stenosis, and in 23 with transposition of the great trunks. As an isolated condition it is among the more infrequent of cardiac anomalies. The first carefully recorded case of primary patency with autopsy findings, was diagnosed before death and published by Bernutz¹ in 1849. Six cases were collected by Almagro² in 1862, 12 by Gerhardt³ in 1867, 20 by Wrany⁴ in 1871, and 26 by Vierordt in 1898. Herxheimer enumerated all the above in 38 cases collected in 1910, while Wells,⁵ in 1908, found 41. A careful analysis of 34 cases with, and 37 without, autopsy report was published by Goodman⁶ in 1910, and there are important clinical studies by Hochsinger, Gillett,⁷ Taylor,⁸ and Wessler.⁹ From these and other sources, 64 cases of uncomplicated primary patency with clinical history and autopsy reports, have been analyzed in this series. Of these, 18 are in infants under two years, and 46 in "adults" over this age. As of special interest, or not included by other writers, may be mentioned the cases by Hewitt,¹⁰ Hall,¹¹ Kingsley,¹² Thompson¹³ and Carpenter¹⁴ in infants; and Kaulich,¹⁵ Fagge,¹⁶ Darier,¹⁷ Schrötter,¹⁸ Drasche,¹⁹ Garipuy,²⁰ Crouzet,²¹ Greenhow,²² Gibson,²³ Wells, Schnitzler, and Mead,²⁴ in adults, as well as 13 adult cases quoted below, in which the patency was complicated by acute infective pulmonary endarteritis.

Pathogenesis.—The causes of persistent patency of the duct are to be sought in the conditions of its normal closure, and this must depend upon the influences, mechanical or otherwise, of the changes in the circulation at birth, and upon the consequent alterations in the vessel wall, itself a fetal structure destined to involution. As *possible factors* in the process of closure may be enumerated: (1) peculiarities in the histological structure of the ductus wall, (2) alterations in the blood-pressure at birth, (3) modifications at birth in the position of the ductus relative to the aorta and pulmonary artery, and other mechanical factors preventing entrance of blood from the aortic side.

1. *Histology.*—The ductus wall is poor in elastic tissue as compared with the aorta and pulmonary artery, but is relatively rich in muscular elements, which, as well as the elastic tissue are known to undergo marked increase during the later months of intra-uterine life. More

¹ *Arch. Gén. de Méd.*, 1849, xx, 415.

² *Thèse de Paris*, 1862, p. 67.

³ *Jena. Zeitsch. f. Med. u. Naturwis.*, 1867, Bd. iii.

⁴ *Oestr. Jahrb. f. Pädiatr.*, 1871, Bd. i, p. 1.

⁵ *Am. Jour. Med. Sc.*, 1908, pp. 136, 381.

⁶ *Univ. of Penn. Med. Bull.*, 1910, xxiii, 509.

⁷ *Gaz. d. hôp.*, 1910, 83, p. 1419.

⁸ *Guy's Hosp. Gaz.*, May, 1901, p. 197.

⁹ *Am. Jour. Med. Sc.*, 1913, cxlv, 543.

¹⁰ *Trans. Path. Soc. London*, ix, 48.

¹¹ *Arch. Middlesex Hosp. Clin.*, Series XIII, 1913, p. 39.

¹² *Johns Hopkins Hosp. Bull.*, 1911, xxii, 239.

¹³ *Edin. Hosp. Reports*, 1900, vi, 57.

¹⁴ *Proc. Roy. Soc. Dis. Ch.*, 1909, ii, part 1, p. 163.

¹⁵ *Viert. f. prak. Heilk.*, 1862, ii, 92.

¹⁶ *Guy's Hosp. Reports*, 1873, xviii, 22.

¹⁷ *Bull. de la Soc. Anat. de Paris*, 1885, x, 55.

¹⁸ *Zeit. f. klin. Med.*, 1901, xliii, 161.

¹⁹ *Wien. klin. Woch.*, 1898, xi, p. 1195.

²⁰ *Bull. de la Soc. Anat.*, February, 1907, p. 179.

²¹ *Ibid.*, 1869, xiv, 323.

²² *Clin. Soc. Trans.*, 1876, ix, 152.

²³ *Edin. Med. Journ.*, 1900, n. s., viii, 1, 212, 436.

²⁴ *Jour. Am. Med. Assn.*, December 24, 1910.

particularly a loose, subintimal layer of muscle is present (Thoma¹); this evidently corresponds to Jore's musculo-elastic layer of the arterial wall, which is here developed both at an earlier period and to a greater extent than in the aorta and pulmonary artery. It is especially marked at either extremity of the duct where it can be seen to pass into and, indeed, to form, the musculo-elastic layer of the aorta (Klotz). When the canal is emptied of contents, as happens after birth, this increased muscularity enables it to contract firmly, so that its walls remain in juxtaposition and may undergo obliterative endarteritis.

2. *Alterations in the Blood pressure at Birth.*—Previous to birth, the pressure is highest in the right side of the heart; the pulmonary arteries are small, and almost all the blood passes through the ductus into the aorta. At birth the lungs are expanded, their capillaries are opened, and there is an immediate lowering of pulmonary blood pressure. Dr. Adami suggests that during the first few days of life the aortic tension, and therefore the mean blood pressure in the body as a whole, is also lowered, owing to the reduced amount of work which the heart is called upon to perform, after the cutting off of the placental circulation, and that this reduction in the mean blood pressure is the cause of the collapse of the ductus, and the main factor in closure. Kirstein also believes that a pressure equilibrium is established between the aortic and pulmonary circulations, which prevents a current through the ductus and thus permits of its obliteration, while Klotz thinks that alterations in the pulmonary pressure at birth, and the relative muscularity of the ductus wall are together sufficient to account for closure.

3. Nevertheless, *mechanical conditions preventing the flow of blood through the ductus from the side of the aorta* have been adduced by many workers, and may reasonably be supposed to assist in the process of closure, especially when the pressure in the aorta comes to exceed that in the pulmonary circulation. Schantz supposed a stretching of the duct by the movement of the pericardium, pulmonary artery, displaced thoracic organs, and sternum, in the initial respiration, and Strassman described, on the basis of a large number of injection experiments, a fold in the aortic wall at the upper border of the mouth of the duct, which appears about the seventh month, and which he thinks closes its opening in a valvular manner when the pressure rises in the aorta at birth. This theory of a valvular aortic fold has been widely accepted and has received recent confirmation in the experimental work of Fromberg.² Nevertheless, its constancy in infants, and its valvular action when present, has been gravely disputed by such careful observers as Klotz, Kirstein and Stiènon.³ The last word on this subject has come from Stiènon, who has found that Strassman's fold is not shown on plaster casts of the ductus and adjacent vessels in the newly born, made under low pressure, and ascribes its appearance postmortem to the falling together of the canal after its evacuation. From the study of a large number of such casts of the aortic isthmus and of patent ductus at

¹ *Virchows Archiv*, 1883, vol. xciii, 443.

² *Baumgar. Arbeit. aus. d. Geb. d. Path.*, 1914, ix, 198.

³ *Archiv. de Biol.*, 1912, xxvii, 801.

various ages, he concludes that the essential mechanical factor in closure is the *dilatation of the fetal isthmus*, which is produced by raised aortic tension after birth, so that the latter has the secondary effect of favoring closure by pressure of the dilated isthmus on the aortic end of the duct. Dislocation of the thoracic organs in the establishment of respiration probably also assists in diverting the circulation.

From the above considerations the general conclusion may be drawn that continued patency will occur (1) in conditions in which the blood pressure, either in the aorta or pulmonary artery, is maintained at a level approximating that before birth (as in atelectasis of the lungs), or in which, for any other cause, a high positive pressure in the ductus is maintained; (2) when a congenital defect in the structure of the ductus wall exists. That such a defect is not uncommonly the cause of patency is suggested by the frequent association of anomalies elsewhere in the body and by the not uncommon occurrence of a history of syphilis, or of anomalies in other members of the same generation, as in De la Camp's remarkable series of six brothers and sisters all with characteristic physical signs of patent duct.

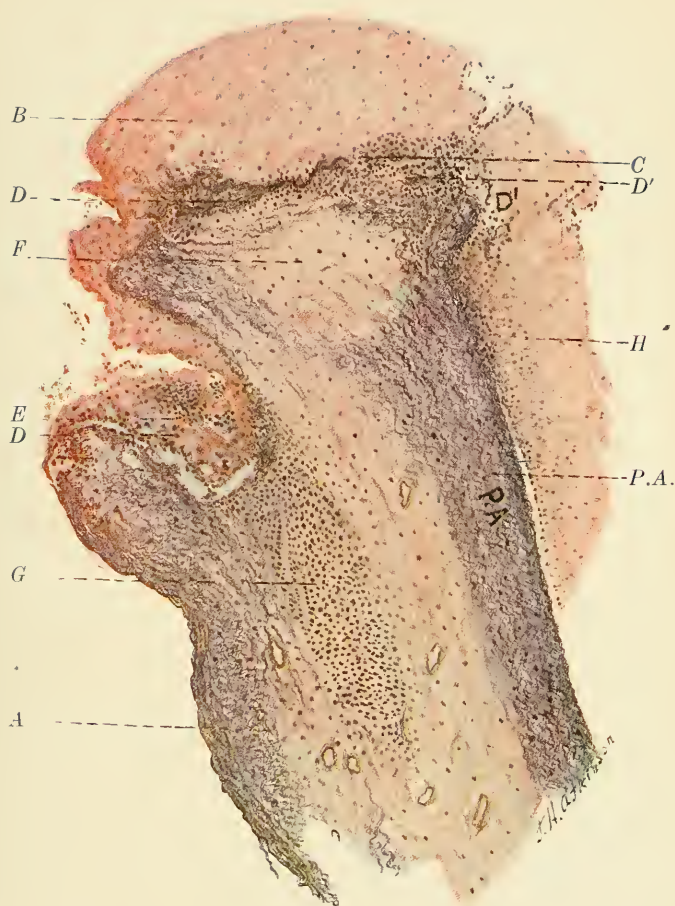
That raised pulmonary pressure is usually at fault is evidenced by the frequent history of atelectasis of the lungs, difficulty in suckling or prolonged delivery in the mother, seen in the present series. In support of Stienon's view, that dilatation of the fetal isthmus is an important factor, we may note that persistent patency is associated in most adult cases with a certain degree of coarctation of the aorta, and that the process of closure after birth is, like dilatation of the isthmus, a gradual one, extending over the first weeks of life and often not completed until the third month.

Pathology.—Three principal types of patency may be distinguished: (1) The duct may be greatly shortened upon itself so that its ends are approximated to each other, and it disappears as a canal, remaining as a simple aperture between the two great trunks. (2) More frequently the ductus persists as a short canal from 0.4 to 2 cm. long (Vierordt), with a lumen varying in size from one just admitting a bristle to one allowing the passage of a "goose-quill," "pencil," or even, as in Luys' case, the "finger." A patent ductus of long standing is usually shorter and broader than that of infancy or later fetal life. In form this canal may be (*a*) cylindrical, as is usual in infants, and as was seen in the cases by Fagge, Almagro, Gerhardt, and White¹ in adults; or (*b*) funnel-shaped (*i. e.*, conical, as in a funnel without a stem), with its larger end toward the aorta, as in a case by Murray, in which in a woman aged thirty-six years, it formed a truncated cone three-eighths of an inch long, just admitting a quill, and lying with its base to the aorta. Finally (following Gerhardt's classification into four types, of which the above forms 1, 2*a* and *b* constitute the first three), the patent duct may exist (3) as a canal which has undergone aneurismal dilatation.

In a patent ductus with otherwise normal conditions, the blood stream will be directed chiefly from the aorta, where the blood pressure is

¹ *Trans. Path. Soc.*, London, 1885, xxxvi, 182.

PLATE VI



Microscopic appearances of wall of patent ductus and adjacent aorta and pulmonary artery in a case of patent ductus arteriosus with acute infective pulmonary endarteritis, showing site of initial lesion at pulmonary end of ductus. Drs. Hamilton and Abbott. (Colored drawing by Dr. J. H. Atkinson.) (Haem. and eos. and elastic tissue stains. Low magnification.) A rectangular block has been cut to include the whole wall of the ductus (*D, D'*) and a portion of the pulmonary artery (*P.A.*) and aorta (*A*) adjacent. *A*, wall of aorta which is quite healthy. *P.A.*, wall of pulmonary artery. *D, D'*, wall of ductus arteriosus in which the elastic tissue is almost destroyed, and which is surmounted by a thrombotic mass (*B*). *C*, pulmonary end of ductus, showing destruction of elastica, and organization of inflammatory products (*i. e.*, seat of initial lesion). *E*, aortic end of ductus showing zone of recent inflammatory exudate and invasion of tissue between aorta and pulmonary artery by acute inflammation. *F*, necrosed area below ductus wall. *G*, recent acute inflammatory process extending from aortic end of ductus into cellular tissue between aorta and pulmonary artery. *H*, thrombotic mass overlying wall of pulmonary artery and becoming incorporated with it in neighborhood of pulmonary end of ductus.

higher, into the pulmonary artery. This is evidenced by the funnel-shaped form with its base toward the aorta, which the canal usually assumes in adults, and by the presence of mycotic vegetations on the adjacent wall of the pulmonary artery in all the cases of acute infective endarteritis in the neighborhood of a patent duct. Wagener's 3 cases, in which the membrane at the pulmonary end bulged into the artery, also indicate this direction of the stream. Dilatation of the pulmonary artery, and hypertrophy and dilatation of the right ventricle, are usual results of patency of long standing. Rauchfuss thought them characteristic of all cases, but exceptions occur. The left ventricle may share in the hypertrophy and the aorta be moderately dilated. In Fagge's case, a woman aged forty-two years, the right ventricle was greatly hypertrophied, being equal to the left in thickness; the right auricle was dilated, and the main pulmonary branches, especially the right, were much dilated. The left ventricle is occasionally hypertrophied in excess of the right. In rare instances, as in Walsham's and Drasche's cases, aged respectively forty-seven and twenty-nine years, the heart may not be hypertrophied at all.

Arteriosclerotic patches are not uncommon in the neighborhood of the patent duct in the aorta, and extensive atheroma may occur also in the pulmonary artery. In Hebb's¹ case the atheroma and dilatation of this trunk seem to be explained rather by the obliteration of its left branch through the pressure of the thrombosed duct.

Durno and Brown,² report a case in a man of thirty-three, of widely patent ductus arteriosus, with extensive atheroma both of the walls of the ductus, and of the greatly dilated pulmonary artery. A small saccular aneurism of the pulmonary close to the ductus had ruptured, forming a dissecting aneurism which in turn burst into the pericardium.

Acute Infective Pulmonary Endarteritis.—Vegetations of a malignant character are not uncommon within a patent duct, about its aortic orifice, and on the adjacent wall of the pulmonary artery. There are 13 such cases in our series; in all, the pulmonary artery adjacent to the ductus was extensively diseased, and in all but one (Hamilton and Abbott³), the heart valves were also involved in a malignant endocarditis. This last case was of especial interest because of the strict localization of the infective process to the ductus and the pulmonary artery adjacent, which showed clearly that the acute inflammatory process had originated in the immediate neighborhood of the defect, a point confirmed by microscopic examination, in which the organization of the inflammatory products proceeding at the pulmonary end of the ductus was clearly seen (see Plate VI), thus demonstrating this to have been in all probability, the earliest initial seat of a process, which had elsewhere and later assumed a fulminating, highly destructive character.

The patient was a girl of nineteen years, who presented a clinical picture of septicemia for some weeks before death, and the characteristic physical signs of patent ductus, without valvular involvement, or cyanosis. Postmortem a huge thrombotic mass of vegetations lay in the lumen of

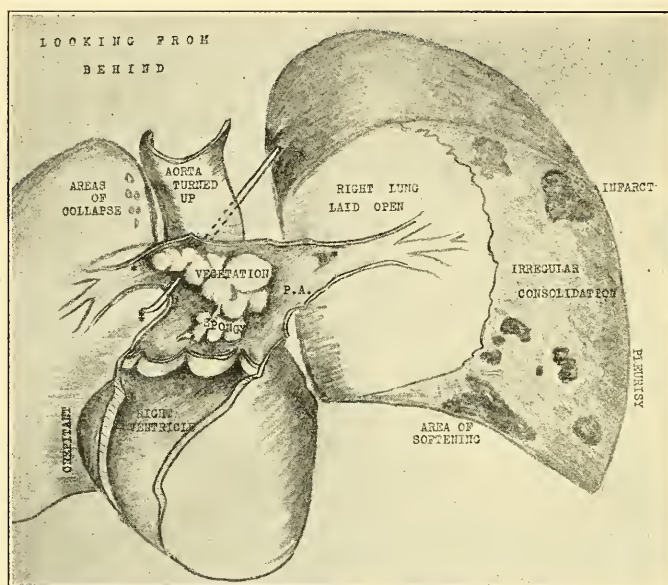
¹ *Trans. Path. Soc.*, London, vol. xlv, 45.

² *Lancet*, 1908, i, 1692.

³ *Trans. Assoc. Am. Phys.*, 1914, vol. xxix (gives full bibliography).

the dilated pulmonary artery blocking the orifice of a large patent ductus, and extending into the left pulmonary artery (see Fig. 38). The aorta was stenosed at the isthmus but was otherwise healthy and the endocardium of the heart was free from every trace of disease. Embolic abscesses in the lungs, the vegetations in the pulmonary artery, and the blood culture during life contained swarms of pneumococci. Both the patent ductus and pulmonary endarteritis were diagnosed during life.

FIG. 38



Diagrammatic drawing showing acute vegetative endarteritis of pulmonary artery in the neighborhood of the patent ductus arteriosus, and consequent infarcts of the lung. A probe is seen passed through the patent ductus. (W. F. Hamilton and M. E. Abbott.)

The wall of the aorta opposite the ductus was the seat of the mycotic vegetations in some cases, indicating that the infection had proceeded with the current through the ductus and had impinged here.

Paradoxical Embolism.—In Schmorl's¹ case, an embolus passed from a primary thrombus in the left auricle, through a patent ductus arteriosus to the pulmonary artery. In the cases of acute infective pulmonary endarteritis enumerated above, septic infarcts in both systemic and pulmonary circulations, evidently from emboli passing through the patent ductus, were extremely common, occurring even in those cases in which only the tricuspid valve and pulmonary artery were diseased. Hochhaus based a correct diagnosis upon this feature.

Symptoms and Signs.—Clinical evidence of patency of the ductus is to be sought rather in physical signs than in symptoms, for the latter are often obscure. Nevertheless, their very negative character when

¹ *Verhandl. d. deutsch. path. Gesellsch.*, 1909, xiii, 217.

taken in combination with the distinctly characteristic physical signs, presents, in the majority of cases, adequate grounds for a correct diagnosis, and this can almost always be made. Careful contributions are now numerous, and a symptom complex has been built up which makes this chapter in congenital defects almost as legible to the clinician as that of any form of acquired cardiac disease. On account of the secondary anatomical changes that are usually induced in a patent ductus of long standing, such as shortening and widening of the duct and dilatation of the pulmonary artery, the picture in infants and early childhood, is somewhat different, and much less distinctive than that in later life. This statement applies especially to the physical signs.

The typical appearance is one of anemia, sometimes profound, which has been described as wax-like. Cyanosis is usually absent; when present it is generally slight and transient, appearing only on exertion, and usually develops late, sometimes as a terminal event. Of the 57 cases in which this point is mentioned, cyanosis was entirely absent in 27, of which 19 were in adults and 8 were in children under two years. Cyanosis was noted as slight in 13 cases, in one of which, Bittorf's (aged eleven years), it was constant, in the others transient, appearing only on crying in Simmons' (aged sixteen weeks), and during anginal attacks in Hale White's case (aged fifty-three years). It was moderate in 4 cases only. In that by Carmichael, dying at three, it came on soon after birth, becoming extreme, with clubbing and a polycythemia of 8,100,000. Coarctation of the aorta was associated with the patent duct, and mitral stenosis with great dilatation of the left auricle was present as well, suggesting a rise of pressure in the pulmonary artery and a possible reversal of flow, venous blood from this vessel entering the aorta through the canal.

Dyspnœic attacks usually accompanied by transient, but marked cyanosis, are relatively common in infants and are so characteristic of these cases that the name *La Cyanose Congénitale Paroxystique* has been proposed. Loss of consciousness may occur during the attack and the heart may stop beating, or death may supervene. Three typical cases were reported by Hall in infants, all of whom died during the attack, and others by Sanders, Carmichael, Luys, and Bommer.¹ In the latter (aged sixteen weeks) the cyanosis was transient, coming on only during the attacks, which came on especially during feeding, and recurred at last so frequently that the child failed for lack of nourishment; during the attacks the breathing stopped suddenly and deep cyanosis developed, lasting two to four minutes; it passed off entirely as the breath returned, in the interval the color being normal. This is very suggestive of an admixture of venous with arterial blood as the cause of temporary cyanosis, the pressure becoming higher in the pulmonary artery and lower in the aorta during the act of suckling.

In older subjects cardiac seizures of various sorts may replace these suffocative dyspnœic attacks. Paroxysms of extreme tachycardia (pulse 200), with dyspnœa and bloody expectoration, lasting for some

¹ *Freiburg Thesis*, 1900.

hours, and recurring every few months, are described in a man aged thirty-six years, with dyspnœa and palpitation on exertion for years, but no cyanosis (Bommer). Hale White reports repeated angina-like attacks, in one of which death occurred, in a man aged fifty-three years, with a patent duct the size of the anterior tibial artery, but no hypertrophy of the heart or disease of this or of the aorta.

Epistaxis, hematemesis, and hemorrhages from other mucous surfaces are not uncommon (Almagro, Carmichael, Darier, Duroziez). Unless death occurs from some intercurrent condition, as malignant endocarditis or endarteritis, the patients usually die with failing compensation, and dyspnœa is a remarkably constant feature. Sudden death occurred in eleven cases in our series; in six during dyspnœic attacks, in three, those by Reid, Crouzet and Chessman, without apparent cause, in the case by Mead from rupture of the heart and in that by Durno Brown from rupture of the pulmonary aneurism above described.

Physical Signs are almost invariably present, and are usually characteristic in older patients. In infants they are practically indistinguishable from those produced by auricular and ventricular septal defects. This is because the patent duct is at first a straight canal, which does not allow of the passage of a large volume of fluid and because in the absence of dilatation of the pulmonary artery there is less sound produced by the impinging of currents in this situation. Among our 64 cases physical signs were absent in only 8 cases. Absence of physical signs in the case of Walsham, quoted by Vierordt in this connection, must be pronounced doubtful, for the specimen came from the dissecting-room with an indefinite note that cyanosis and pericardial murmurs existed. A negative finding in the cases by Luys and Duroziez was also disputed by Almagro.

The distinctive physical signs (which develop as life proceeds), as well as the absence or late appearance of cyanosis, depend, as Gerhardt pointed out, on the fact that a patent duct of long standing usually has a short, wide lumen through which during systole blood flows freely from the aorta into the pulmonary artery, which dilates accordingly and becomes, with the ductus itself, the chief seat of whatever vibration or murmur the abnormal current may produce; the right ventricle behind it usually undergoes hypertrophy and dilatation as well. Gerhardt described as characteristic a visible systolic pulsation in the second left interspace (indicating the forcible closure of the pulmonary valves), an increased area of cardiac dullness, especially to the right, and a narrow zone of dullness 3 to 4 cm. wide (corresponding, he believed, to the dilated pulmonary artery) lying at the base of the heart, along the left sternal border from the third to the second or first rib, and extending a little way over the first piece of the sternum. This "ribbon-shaped" dullness has been noted by many other observers, and has recently been strikingly confirmed in a number of cases in which Gerhardt's dull area, with characteristic murmur or thrill localized over it, has been found by the x-ray to correspond with a pulsating shadow lying above the base of the heart, which was evidently from its size and position the dilated pulmonary artery. In Bittorf's case this shadow was seen, when looked

at from the side, to be the size of a walnut and to pulsate a little later than the heart and synchronously with the aorta. In Arnheim's case the *x*-rays showed, besides enormous hypertrophy of both sides of the heart, which occupied nearly the whole left thorax, the greatly enlarged shadow of the pulmonary artery placed above the cardiac shadow "like a cap," and numerous tortuous dilated vessels, indicating an extensive collateral circulation and a probable coexisting coarctation of the aorta. In the cases reported by Schrötter, Mead, and Hamilton and Abbott, the *x*-ray cap, and Gerhardt's dulness, were found at autopsy to correspond with the dilated pulmonary artery.

When cardiac hypertrophy is marked, precordial bulging, diffuse pulsation, and other evidences will be present. An increased area of cardiac dulness, especially to the right, while usual, is not invariable, for the left ventricle may be hypertrophied in excess of the right (Murray's case), or in rare instances there may be no cardiac hypertrophy at all (Drasche's case).

A *thrill*, usually systolic, but sometimes continuous through the cardiac cycle, is fairly frequent, and was present in 17 of the 64 cases. It may be diffuse over the precordium, but is usually localized to the neighborhood of the second left interspace, in the region described above as Gerhardt's dull area, or at least is of maximum intensity here. Its transmission obliquely upward below the clavicle (along the course of the pulmonary artery) is said to be pathognomonic.

The auscultatory phenomena are the most important and constant. In infants a harsh systolic murmur with more or less of the above localization is the rule, but in adults a loud murmur is nearly always produced, which is characterized by almost all observers as peculiar, and is variously described as harsh, musical, scraping, scratching, humming, churning, rushing, rolling, and only rarely as blowing. Müller compares it in his case to "rolling thunder," and says that two different listeners likened it independently to the noise made by a train in passing through a tunnel, and Thayer described it in Mead's case as a "machinery murmur." In rhythm several different types may be made out: (1) The murmur is frequently systolic (as in the cases by Murray, Halé White, Simmons, and Bittorf). (2) It may begin with systole, but continue into and through diastole, either as a continuous hum (Chessman's case), or with a systolic rise (Bommer), or with a rhythmic systolic, and diastolic accentuation. Gibson¹ describes as pathognomonic a continuous, rushing murmur which "begins distinctly after the first sound, accompanies the latter part of that sound, occupies the first pause, accompanies the second sound (which may be accentuated in the pulmonary area, or doubled), and finally dies away during the long pause." (3) Sometimes, as in Drasche's case, two independent murmurs are heard at the pulmonary area, the loud, peculiar, systolic one, and a low, short, diastolic, indicating a slight regurgitation into the aorta during the pause. (4) More rarely the murmur is diastolic in rhythm, as in Fagge's case, in which a diastolic murmur, musical and of a wavy

¹ *Medical Press and Circular*, May 30, 1906.

character, was localized to the pulmonary cartilage. The point of maximum intensity is usually in the second or third left interspace, and it is often heard very loudly in the first left interspace below the clavicle and over the first part of the sternum and in the back to the left of the third and fourth dorsal vertebræ, and in the left suprascapular region. In Franck's case and in one by Gillet, the murmur was only heard posteriorly in this situation, and not in front at all. It is transmitted over the left ventricle, and its systolic element often is audible over the carotids, sometimes more distinctly over the left than over the right (Gerhardt). It may diminish abruptly below the third left costal cartilage. In this series of 64 cases, among the 18 cases in infants, in 8 a systolic, and in 1 a continuous murmur was present. Among the 46 adults, in 19 cases the murmur was systolic, in 9 "double" and in 14 it was the continuous "harsh," "rumbling," "rolling," "churning," "humming" murmur usually with systolic accentuation, described by the earliest students of this subject as characteristic, and which Gibson rightly described as pathognomonic.

Franck mentions, as of diagnostic value, an inspiratory accentuation and an expiratory diminution both of the characteristic murmur and of the radial pulse (*pulsus paradoxus*), which they explain by saying that during respiration the pressure in the thorax is lowered, so that more blood can enter the pulmonary artery than during expiration, and this will lead to a smaller pulse wave from the aorta, to a larger current through the canal, and a correspondingly louder murmur.

The second pulmonary sound is frequently much accentuated, and this is very important as distinguishing patency of the duct from pulmonary stenosis with somewhat similar localization of murmur or thrill. On the other hand, in some cases it may be weak or even inaudible.

In the cases by Schrötter and Mead *paralysis of the left recurrent laryngeal nerve* was present, due to pressure upon the nerve by the enlarged patent duct. Schrötter based a correct diagnosis on this feature. The nerve was degenerated on microscopic examination.

The physical signs are very often obscured by those of other lesions, as malignant endocarditis or arteritis, chronic valvular disease, or other cardiac anomalies so commonly associated. The peculiar character of the murmur, its more or less prolonged rhythm, its localization, and that of the thrill when present, high up toward the left infraclavicular region, with the results of x-ray examination, remain, even in these complicated cases, of the first diagnostic value. Patent duct must be diagnosed also from perforation of the aorta and pulmonary artery just above the semilunar valves, whether of inflammatory or congenital origin. Brocq¹ gives a long series of cases of both types.

So-called aneurisms of the ductus Botalli give rise to no physical signs, being of small size and usually occluded by thrombus. They are generally said to be of little clinical significance, but death from rupture of their walls has been reported and embolism from the thrombus within may lead to a fatal result.

¹ *Rev. de Méd.*, 1886, vi, 786.

So-called Aneurisms of the Ductus Botalli.—This term is used in the literature with a rather irregular application to denote a dilatation in whole or in part of a persistently patent duct. That the cases are not aneurisms in the strict sense is inferred by most writers. Rokitsansky uses the qualifying word “so-called.” Gruner says that arterial dilatation would often be a better word, as there is usually no change in the vessel wall, and he draws attention to the fact that in the usual bean-shaped form the constriction at either end makes the ductus appear larger to the eye than it really is. Klotz has suggested that, as in his injection experiments the duct is seen to be much larger at birth when distended with fluid than when contracted at the autopsy, many of these small, so-called aneurisms, measuring less than 1 cm. in their greatest diameter, are really not even a dilatation, but are a simple distension of a patent duct to its full capacity by the coagulum within. Again, a further confusion exists in that the term is applied more widely by some writers than by others. Nevertheless, the cases recorded form a fairly well-defined group, which, from their rarity and from the fact that the duct is usually occluded by thrombus, are chiefly of pathological interest, although their occasional rupture, and also the risk of embolism from the thrombus within, increase their clinical significance. The first cases reported were by Billard, Thore, and other French writers; Rokitsansky followed with his monograph in 1852, and Virchow in 1856; full studies of the literature with original cases are to be found in the theses of Westhoff,¹ and Gruner.²

In what may be taken as the classical form (which is that described by Rokitsansky) the ductus forms a spherical or ovoid tumor larger at the middle than at either end, but smallest toward the pulmonary artery, with which, as well as with the aorta, it communicates, filled with old or recent thrombus, and varying in size from a “cherry stone” (Billard) to a “hazel nut” (Thore), or even a walnut (Hebb, Binzer). In Hebb’s case,³ in a man aged forty years, an aneurism the size of a small walnut, filled with old clot, lay in the position of the duct, communicating with the aorta by an orifice one-eighth of an inch in diameter, and abutting against the obliterated left pulmonary artery and left bronchus. All the cases recorded are in infants excepting that by Hebb.

In Thoma’s⁴ patient, aged twenty-six years, the aorta, from the isthmus downward for about 4 cm., was dilated in the form of a spindle, was lined by atheromatous plaques, and on its right wall opposite the left subclavian artery was a saccular aneurism, in the floor of which lay a small hole representing the lumen of the greatly shortened ductus leading into the pulmonary artery, which was here firmly adherent to the aorta. Microscopic examination showed this aneurism not derived from an expansion of the aortic end of the ductus, but to be a bulging of the aortic wall, which the writer thought was pulled to the right by the action of the contracted ductus. Rokitsansky’s 5 cases of funnel-shaped patency were explained by Thoma in the same way, and a special form of “traction aneurism of the infantile aorta” was thus established by

¹ *Göttingen Diss.*, 1873 (quoted by Gruner and Voss).

² *Freiburg Diss.*, 1904.

³ *Trans. Path. Soc.*, London, 1893, xliv, 45.

⁴ *Virchows Archiv*, 1890, Bd. 122, p. 535.

him. In Wagener's 3 cases, aged respectively thirty-eight, forty-two, and twenty-three years, the duct formed a distinct canal with a small lumen open on the side of the aorta, where the orifice lay in the floor of a hollow in the wall of this vessel, and was sheltered by a distinct fold of aortic intima projecting downward from above while the pulmonary end was closed in by a thin membrane, which bulged into the pulmonary artery. Mycotic aneurism of the patent duct of the dissecting form has been described by Buhl.

Absence of the Ductus.—Absence of the ductus may occur, and is usually associated with hypoplasia and shortening, sometimes with atresia, of the pulmonary artery. It is explained as due to a primary failure of development of the sixth left branchial arch (which persists as the ductus), the stenosis of the pulmonary being secondary. In these cases a septal defect is present, through which the aërated blood passes from the right heart to the aorta.

Anomalous Course.—Multiple origin is reported by Peacock in a case of pulmonary stenosis, two small trunks arising at the site of the normal ductus and passing, the smaller into the left, the larger (which was cut short) apparently into the right pulmonary artery. In several cases the canal has opened into the left subclavian. In one case, of right aortic arch, the duct entered the descending aorta below the right subclavian and itself gave off the left subclavian artery.

COARCTATION OF THE AORTA.

This term applies to a well-recognized group of cases in which there is a narrowing or stenosis, amounting sometimes to a complete obliteration, of the descending arch at, or immediately below, the so-called isthmus of the aorta, which is that part of this vessel lying between the left subclavian artery and the insertion of the ductus arteriosus. During the period of fetal circulation this segment is comparatively little used, and at birth is usually observed to be of slightly smaller lumen than the adjacent portions of the aorta, the difference soon disappearing under normal conditions. Thérémín states, as a result of his measurements of the normal infant heart, that in 80 per cent. a slight diminution in diameter exists in the isthmus during the first three months of postnatal life, after which a calibre uniform with the remainder of the arch is attained; and that in some 6 per cent. a slight difference remains throughout life which he does not consider abnormal unless it amounts to more than 2 mm. Bonnett classed as anomalous those cases in which the difference was about 3 mm.

Two distinct groups of cases are understood under the term. (a) A diffuse narrowing of the aorta at the isthmus (Bonnet's infantile type). In some of these cases in which the stenosis is marked, the circulation in the lower part of the body is maintained by a large patent ductus arteriosus through which *the descending aorta appears to be a direct continuation of the pulmonary artery*. Such cases, being essentially the same in origin as coarctation, may be included with it. (b) A more or less abrupt constriction of the aorta at or near the insertion of the ductus arteriosus (Bonnet's adult type). Here, where coarctation is marked and has

lasted some time, the establishment of an extensive collateral circulation frequently completes the picture and lends distinctive features to what is otherwise an obscure lesion.

Relative Frequency.—The figures in the literature are somewhat misleading, for curiously little account is taken of its occurrence by many workers, and therefore the lesser degrees of coarctation are probably often overlooked in the postmortem room, and cases with well-marked vascular changes may escape diagnosis at the bedside. On the other hand, this subject has been so carefully worked over and brought up to date by successive writers, that its statistics are clearer and more accessible than is the case perhaps in any other chapter of congenital cardiac disease. Very probably, therefore, the 212 cases enumerated here are not far from being the full number recorded, whereas the total number of pulmonary stenosis or of septal defect (which anomalies have not been subjected, at least of recent years, to such careful repeated statistical analysis) must be much higher than that given by any author. For this reason Vierordt's statement that coarctation ranks next in frequency to pulmonary stenosis is probably placing the incidence too high. A truer estimate may perhaps be gathered from the fact that among 205 cardiac anomalies recorded in the *Transactions*, there are 22 of stenosis or obliteration of the aorta at the isthmus and 2 of entire absence of the aortic trunk between the left subclavian and the ductus, against 91 of pulmonary stenosis and 165 defects of the interventricular septum.

The first case was reported by Paris in 1789. Craigie collected 10 from the literature in 1841, von Leeuwen 18 in 1850, Rokitsansky 26 in 1852, and Peacock 46 cases in 1866. Barié,¹ in 1885, gave a review of 89 cases, in which he published the series of the above authors, with others from the literature. The fact that 6 of these are without autopsy findings reduces the number of Barié's cases for statistical purposes to 83. Schichhold, in 1897, added 30 to these, and Vierordt, in 1898, brought the number of recorded cases to 126. In 1903, Bonnet² published an article analyzing Barié's findings, and adding to these a synopsis of 77 additional cases which include the series of Schichhold and Vierordt, make, together with the 83 cases collected by Barié, a total of 160, of which 55 are in infants and 105 in adults. In addition to Bonnet's 160, the writer³ has collected records of 52 cases not included by the

¹ *Révue de Médecine*, 1886, vi, 501.

² *Révue de Médecine*, 1903.

³ Of these 52, 15 are from a series of 18 cases collected by Fawcett from *Guy's Hospital Reports* and published in 1902; 12 are from the *Transactions* reported by Chevers (vol. i, p. 55), Rees (vol. ii, p. 203), Peacock (vol. vii, p. 83), Lees (vol. xxi, p. 58), Wilkes (vol. xi, p. 57), Smith (vol. i, p. 52), Barlow (vol. xxvii, p. 41), of coarctation in infants, and by Peacock (vol. xii, p. 38), Finlay (vol. xxx, p. 262), King (vol. xxiii, p. 83), Habershon (vol. xxxix, p. 71), Mackenzie (vol. xxx, p. 66), in adults.

The remainder are reported by Preisz (*Jahrb. f. Kinderheilk.*, xxxiii, p. 140), Lawrence and Nabarro, Hektoen, Dick (*Proc. Clin. Path. Society*, May 9, 1904), Osler (*Montreal Gen. Hosp. Rep.*, P. M. No. 252), Pansch, (*Giessen Thesis*, 1905) in infants, and by Pappenheimer (*Proceedings New York Path. Soc.*, May, 1905, January, 1906, p. 177, October, 1906), Variot, Carmichael, one in *St. Bartholomew's Hosp. Rep.*, vol. i, series I, one in the Museum of Toronto University, in adults, Mönckeberg (2 cases) (*Deut. Path. Gesell.*, 1907, xi, 267), Moon (*Lancet*, June 8, 1912), Rokitsansky (3 cases) (*Krank der Arterien*, 1862, Obs. 21), Sella (2 cases) (*Zieg. Beil.*, 1910, lxix, 501), Strassner (*Deut. Arch. f. klin. Med.*, 1909, lix, 349), Wadstein, 1897 (quoted by Sella), Oberndorfer (*Verh. deut. Path. Gesell.*, January, 1910), MacCallum.

above authors, 15 of which are in infants and 37 in adults, making a total of 212 cases, of which 70 are in the newly born, and 142 in patients over one year.

Pathogenesis.—The proximity of the stenosis to the insertion of the duct in the aorta suggests that the part which this vessel takes in the circulation, or the changes which go on in its form and tissues during its closure after birth, have an essential bearing on the production of coarctation. Rokitsansky (1852) assumed *in all cases*, as the essential condition, a persistence of the isthmus and a consequent weakening of its walls so that they yielded, in a way the healthy aorta would not do, to the traction exerted upon them by the contraction of the duct in its obliteration. Skoda (1855), made the interesting suggestion that in those cases in which the isthmus was not obliterated at birth as a true anomaly brought about by an atrophy of the corresponding embryonic aortic arch, the tissue of the duct had extended into the wall of the aorta, which thus contracted as part of the same process by which the canal itself is obliterated, and Brunner (1888) supposed the transplantation of free portions of the ductus tissue into the adjacent wall of the aorta to occur, rather than its direct extension.

Bonnet gave the most satisfactory contribution to the subject. He divides the cases of coarctation into two types, according as these occur in the newly born or in adults, for each of which he claims a different etiology:

1. The form described by him as that usually seen in the newly born is a diffuse narrowing of the isthmus, and is assumed to be of developmental origin; it is frequently associated with grave anomalies; in it the ductus arteriosus is often patent. The cases in this type fall again into two classes as regards their etiology: (a) When, as in the majority of cases, the stenosis is moderate in degree, it is explained as a persistence of the isthmus at birth, an arrested fetal condition in which this segment fails to attain its normal calibre, and the cause of which is to be sought at or shortly before birth in a simple weakening of the vessel wall, the result probably of a lowered state of general nutrition. Thus Thérémín observed that in the case of his so-called normal infant hearts in which the isthmus was abnormally narrowed at birth, there was a history of premature delivery or of general weakness, and, conversely, that in 50 per cent. of infants born before term or weakly, marked narrowing was present. (b) Those rare cases of the infantile type, on the other hand, with an extreme degree of diffuse stenosis, or in which the isthmus is reduced to an atrophic cord, are probably to be explained, as are also the few recorded cases in which there is a complete absence of the aorta between the left subclavian and the entrance of the ductus, as a failure of development in early embryonic life of that part of the fourth left branchial arch which corresponds to the isthmus of the aorta.

2. Bonnet places in a second class as the adult type those cases seen usually after infancy is passed, in which the coarctation consists of a more or less abrupt constriction of the aorta at or near, often a little below, the insertion of the ductus. This condition, which is never seen in the fetus, nor at birth before the closure of the ductus has begun, is,

he thinks, not of developmental origin, but is to be explained on Skoda's theory of an extension of the peculiar tissue of the duct into the adjacent wall of the aorta, which thus contracts after birth along with the contraction of the arterial canal. As the malposed tissue is scanty and tends to be of a width corresponding to that of the narrow ductus, its contraction will have the effect of a narrow ligature or cord. These cases differ from those of the infantile type not only in the character of the stenosis, but also in that an extensive collateral circulation, giving rise to marked physical signs, usually develops, while serious anomalies are generally absent, this last fact arguing in favor of its postnatal origin. The ductus arteriosus may remain patent, but is usually obliterated.

Associated Anomalies.—The distinction drawn by Bonnet between two types of cases offers a new and significant suggestion. A statistical analysis, on the basis of this division, of the 212 cases available gives interesting confirmation of this statement, and points to a radical difference in the etiology of the two groups. The following figures include as *minor* anomalies occurring chiefly in the adult type, anomalous semi-lunar cusps, irregular origin of the vessels from the arch, patency of the foramen ovale or duct, persistent left superior cava; and as *grave* anomalies, septal defects, transposition of the great trunks, congenital stenosis, etc.

ASSOCIATED ANOMALIES IN COARCTATION IN THE NEWLY BORN (70 CASES).

Series.	Absent.	Minor.	Grave.
Barié	0	3	3
Bonnet	13	11	25
New cases	0	3	12
Total	13	17	40

IN CASES OVER ONE YEAR ("ADULT TYPE") (142 CASES).

Series.	Absent.	Minor.	Grave.
Barié	57	19	1
Bonnet	15	11	2
New cases	8	16	8
Total	80	46	11

Thus among the 70 cases of stenosis in the newly born (dying under one year), in only 13 instances was there no other defect associated; minor defects were present in 17 and in 40 cases grave anomalies co-existed. That is to say, there is frequently associated with the graver cardiac anomalies that form of coarctation which may reasonably be ascribed to a simple arrest of development in later fetal life, and which is due probably to the depressing influences that led to the associated defects, or possibly in some instances to the disturbed circulation that results from the combined anomaly.

On the other hand, among the 142 cases in patients over one year (adult type), other anomalies were absent in 80 instances, minor defects were present in 46, and grave anomalies were associated in only 11 cases; moreover, 7 of these 11 had not the characteristic sharp constriction seen in the great majority of these cases, but were apparently a persis-

tence of the infantile type; for in 3 (Chiari, Houel, MacKenzie) the pulmonary formed the descending aorta through a large patent duct, and the 4 others were in children of two to five years in whom the isthmus was simply diffusely narrowed. Transposition occurred in only 1 (Fawcett), a child aged two years and nine months, with a stenosis apparently of the infantile type. Persistent left superior cava was noted only once (Bonnet).

Equally significant with this rarity of grave anomalies in the adult type of coarctation, suggestive, too, of some etiological factor as yet unknown, is the frequent association in this type of a certain set of minor defects in the structures connected with the aortic arch, namely, irregularities in the origin of the great vessels, absence of the ductus (3 cases), double ductus (Hammernijk), and especially *anomalies of the aortic cusps*, which last are relatively so common as to seem to place their combination beyond the range of coincidence. Thus the *aortic valve was bicuspid* (in itself a rare anomaly) *in 15 instances*; its segments were increased to four with fusion of two of these in one (Fawcett); in one instance (Babington) a small supernumerary cusp had formed on the aortic wall above the others; in two there was subaortic stenosis, in the form of a membranous band below the cusps, and in one there was sub-aortic stenosis and a band of fibrosis with contraction above the aortic cusps.

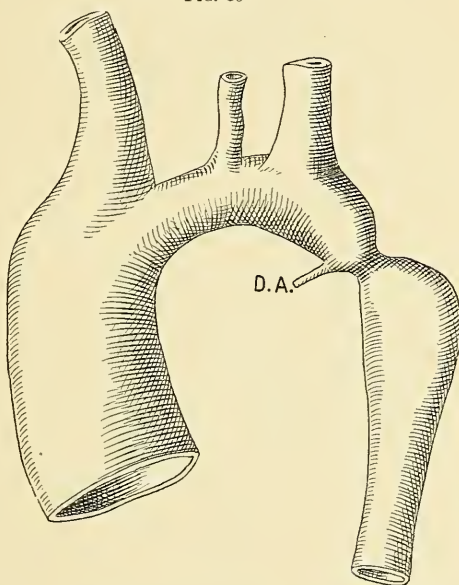
In the infantile type, on the other hand, amid so many grave anomalies, bicuspid aortic valves occurred only twice.

Pathology.—1. The diffuse stenosis of the isthmus usually observed in infancy and always present during the period of the fetal circulation (Klotz), is seen occasionally, but rarely, in later life. It is usually limited below by the ductus, and may begin above as a gradual diminution of the arch, or abruptly at the origin of the left subclavian artery, or, in a few instances, in which the isthmus itself appears to be placed higher up than usual, at the innominate or left carotid artery. The ascending aorta may be dilated or of normal calibre, and below the stenosis the vessel may remain smaller than usual, may return to its full size, or in cases where its descending portion is supplied by a patent duct, be much dilated. The lining of the stenosed area is usually smooth and healthy. In degree it may vary from a mere shade below the normal to a lumen of 1 to 2 mm. in diameter, or be represented in rare instances by a fibrous obliterated cord. Among the total 212 cases, the pulmonary artery formed the descending aorta through a large patent duct in 15 instances, in all of which marked coarctation of the infantile type existed.

2. *Adult Type.*—A very different anatomical character and a much wider variation are presented. In typical cases the aorta is abruptly constricted at the level of, or a little above, or, most frequently, directly below the insertion of the ductus, as though by a tight ligature or cord, the groove thus formed being usually deepest on the convex side of the arch, which appears deeply indented as though cut through in V-shaped manner (Fig. 39). The aorta on either side usually diminishes rapidly toward the stenosis in an hour-glass or funnel-shaped manner, or it may be dilated on either side, giving a sausage-like effect (Bradley). Viewed

from within, the inner surface of the constriction usually presents a projecting ridge or fold corresponding to the zone of constriction without. This may be so marked as to form a distinct septum bridging across the lumen, sometimes obliterating it entirely or leaving a small central circular or triangular lumen, the constriction involving all the coats of the vessel or only its inner ones, the adventitia passing outside of it like a bridge. In other cases the stenosis may occupy a wide area and appear from without like an annular band. Kriejk describes it in his case as a sort of resistant ring, enclosing the aorta like a cuff parallel to the axis of the vessel, and Mannaberg as a solid segment 0.5 cm. long just below the insertion of the duct. The lumen varies through all grades of stenosis down to one just admitting a bristle. In 25 cases of the 142 it was entirely obliterated, in some instances by a septum or diaphragm formed within, but more frequently by the elongated annular form of constriction.

FIG. 39

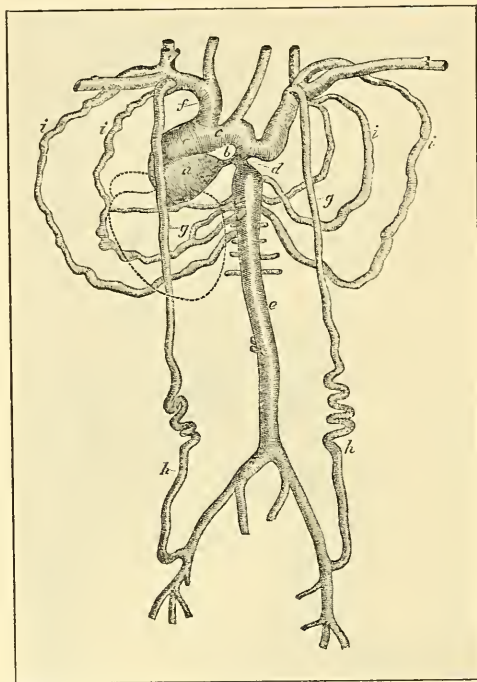


Coarctation of the aorta in a woman aged twenty-seven years. Stenosis beginning just beyond the origin of the innominate artery; sharp constriction immediately below the insertion of the obliterated ductus (D. A.). (Reproduced from Bonnet's article, *Revue de Médecine*, 1903.)

The aorta may be of normal calibre above and below the stenosis, or it may be slightly narrowed at its origin and dilated for a short distance up. The diminution in calibre not infrequently begins at the innominate or left subclavian artery, and in a certain percentage of cases is followed by a dilatation, below which again the characteristic tight constriction near the duct takes place; the effect being that of a *double stenosis*. The aorta immediately below the stenosis is often widely dilated at the seat of origin of the intercostals. *Hypoplasia* of the vessel in its whole length existed in the cases of Hale White, Riegel and Mönckeberg (2 cases). In other cases the aortic walls, otherwise healthy,

are noted as abnormally thin. The aorta may be smooth and healthy in its whole course, as in the cases reported by Brunner (complete obliteration), Cruveilhier, Almagro, Purser, and in the original one by Paris, or there may be extensive atheroma with calcification at the seat of stenosis, above or below it, or throughout the whole aorta. This was present in 39 of the 142 cases, in 9 of which it was definitely stated to be at the seat of stenosis, in 9 localized in the ascending aorta, in 4 localized below the stenosis, and in 7 diffuse throughout the aorta.

FIG. 40



Diagrammatic representation of collateral circulation in a case of coarctation of the aorta: *a*, pulmonary artery; *b*, arterial duct; *c*, arch of aorta; *d*, coarctation of aorta; *e*, descending aorta; *f*, innominate artery; *g*, internal mammary artery; *h*, epigastric artery; *i, i, i, i*, deep-seated arteries of neck and intercostals, forming, together with the internal mammary and epigastric arteries, a collateral circulation with the thoracic and abdominal aorta and internal iliacs. (From Diseases of the Heart and Great Vessels, by W. H. Walshe, London, 1862.)

Rupture of the aorta occurred in 14 cases, in 9 cases at the ascending portion, and in 8 at the seat of stenosis. Aneurism of the arch occurred in 11 instances, and in 8 of these it was of the dissecting form. Sella has made a study of 12 cases of rupture of the aorta, and ascribes its frequent occurrence to the abnormal thinning of the ascending arch, which occurs in many cases of coarctation and which renders the coats more liable to yield under the increased strain.

In most well-marked cases of coarctation of the adult type the blood supply of the lower part of the body is maintained by the development of an extensive *collateral circulation*. The great vessels of the arch are

often enlarged to twice their calibre, and the smaller branches involved are converted into thick, tortuous, dilated trunks. The principal anastomoses are carried on by the superior intercostals, the internal mammaries, and the posterior scapular branches of the transversalis colli *above*, with the first four aortic intercostals, the phrenic and superficial and deep epigastrics *below* the stenosis.

Some evidence of collateral circulation was present in 66 of the 142 cases of the adult type. The particular branches involved and the degree of dilatation vary greatly even in cases of extreme constriction. In 3 instances out of the 142 (Barié, Pic and Bonnamour, and Dubreuil) it was expressly stated to be absent; in most of the remainder the collateral circulation was not mentioned, but this does not imply that it was always absent entirely, as minor alterations in the peripheral vessels are easily overlooked.

The *ductus arteriosus* was patent in 13 of the 142 adult cases. In some instances the ligamentum arteriosum is described as "solidified" or much thickened as though by inflammatory action. Among the 70 cases in infants under one year the ductus was patent 51 times.

Marked *hypertrophy with dilatation of the heart* is rare in infants, but occurs in the majority of the older cases, being noted in 87 out of the 142. It is stated by most authors to be the direct result of the obstruction in the course of the descending arch, but the relation of the two conditions is rendered uncertain by the frequent association of chronic valvular disease, which must be a factor in the hypertrophy. Moreover, a few cases are recorded (*e. g.*, Reynaud's aged ninety-two,) in which, with marked constriction or, even, as in Brunner's case, an obliteration at the insertion of the duct, the heart has remained normal throughout life. This was stated to be the case in 10 of the 142 cases. Although this is a small percentage, it proves that new channels provided for the blood by the dilated collaterals may be sufficient to carry on the circulation without increasing the work of the heart. In Dumontpallier's patient, aged thirty-nine years, in whom the stenosis was produced by a septum with triangular central opening, 13 mm. in diameter, and the heart was not hypertrophied, the collateral circulation was carried on chiefly by the aortic intercostals and the vessels from the subclavian, the anastomosis between the internal mammary and the epigastrics being little developed.

On the other hand, an analysis of the 87 cases with hypertrophy shows that while 50 were complicated with chronic valvular lesions or other cardiac defects, in the remaining 38 no cause was present except the coarctation itself. Of the latter, there were 38 cases of hypertrophy without any assignable cause except the coarctation, hypertrophy was confined to the left ventricle in 9, and involved the whole heart in 30, of which latter the left ventricle especially was enlarged in 9. An interesting point is that in 20 of the 38, the collateral circulation was either stated to be absent or was not mentioned, and in 6 more it was not much developed, the only sign noted being a dilatation of the great vessels of the arch. In the 12 remaining cases a collateral circulation had developed, but in 4 of these the cardiac hypertrophy was only slight.

These facts argue that even in extreme degrees of constriction the heart may remain normal in the presence of an adequate collateral circulation, but that when this becomes insufficient, cardiac hypertrophy and dilatation supervene.

Age and Sex.—A remarkable predominance of the adult type of the anomaly in the male sex is noted by all writers. Among 133 of the 142 cases over one year, 92 were in males, and 41 in females.

That the stenosis does not necessarily interfere with the duration of life is proved by the fact that 9 patients died in the sixth and 9 in the seventh decade, while one (Reynaud's) lived to the age of 92. More than half of the remainder, however (63 cases), died between the ages of twenty and forty years; indicating that, in the anomalous conditions of the circulation that prevail, the system is not, as a rule, equal to the full demands of the stress of normal existence.

In the 142 cases over one year death occurred as follows:

	Cases.
1 to 5 years	7
5 to 10 "	4
10 to 15 "	4
15 to 20 "	17
20 to 30 "	37
30 to 40 "	26
40 to 50 "	16
50 to 60 "	9
60 to 70 "	9
Over 70 "	1
Adults (exact age not mentioned)	12

Symptoms and Course.—Coarctation in infants is of little clinical significance, except in so far as it may complicate other grave anomalies. In the adult type it is a condition of the greatest interest and importance. Symptoms when present may be distinguished as those associated with the lesion and those of the cardiac insufficiency which frequently supervenes. As characteristic of the overtaking of the altered circulation, in which the blood supply to the head and upper extremities is freer than that to the lower part of the body, may be mentioned; violent pulsations (Flaherty's case), plethora with sleeplessness and continuous buzzing in the ears (Légrand), violent headaches (Hammernjk), lividity of the face (Chevers, Purser, Kjellberg), suffusion of the head and neck (Moore), epistaxis and hemoptysis (Flint); in Dubreuil's case, a vascular surcharge of the head and chest contrasted with an atony of the subdiaphragmatic viscera; in that of Redenbacher, a boy aged seven years, with a stenosis at the isthmus admitting a crow-quill, and extensive collateral circulation, the development of the head and upper extremities was in advance of that of the lower part of the body. Severe thoracic, epigastric, or abdominal pain and vomiting of long standing (Roemer's case), or pains in the back or lower extremities (Lebert) occur, and may perhaps be due to the local effect of the constipation. Of significance is Muriel's report of a man aged twenty-five years, who was always weakly, and who developed severe pains in the back and symptoms of aneurism of one of the large vessels of the chest; post-

mortem a dense mass of enlarged glands the size of a hen's egg was found adherent to the aorta at the point of its constriction; it had eroded the dorsal vertebræ. Precordial pain and oppression, dyspnœa, and severe palpitation indicate the cardiac strain. Cyanosis is extremely rare except as a terminal event; in only 2 uncomplicated cases in the whole series (Almagro and Carmichael), in both of which the ductus was patent, was a true congenital cyanosis present throughout life. Lack of development was noted three times, delayed menses once. Many end with a stage of failing compensation, which, in those not complicated by chronic valvular disease, is usually identical with that of mitral incompetence.

Symptoms are (a) absent, (b) late in developing, or (c) present throughout life. (a) In some of the most well-marked cases of constriction or even obliteration at the isthmus, symptoms are absent throughout life. The condition may be quite latent, and constitute, in Barié's words, a "*surprise d'amphithéâtre*" at the autopsy, death occurring from some intercurrent, independent disease. Thus Crisp describes a chance finding of a stenosis admitting a goose-quill in a soldier aged forty-eight years, who had been in excellent health and had died accidentally, and Scheiber complete obliteration of the descending aorta in a man aged forty-one years, dying of pneumonia, who showed no signs of heart disease. In these latent cases sudden death may occur. In most instances a rupture of the heart or aorta is found (Lüttich, Barker, Wise, Legg, and others). Death took place without previous warning or symptoms in 16 of the 142 cases, constituting an event of sufficient frequency to have an important medicolegal bearing.

(b) A large proportion of the cases are in able-bodied, vigorous men, in whom the lesion long remains latent, symptoms developing as the altered circulation becomes overtaxed, or on the intercurrent of some complicating condition, especially endocarditis. Not infrequently, symptoms developing late in life are entirely cardiac in character, cases otherwise latent terminating with a stage of failing compensation which may be due to the lesion itself, or to the chronic valvular disease so often associated.

(c) In a few instances only, symptoms of some obstruction in the cardiovascular system are present throughout life. Quinquaud's patient, a youth aged nineteen years, suffered from infancy with intense palpitation and violent dyspnœa, so that he could not join in play, and œdema of the extremities developed shortly before death, which occurred suddenly. Erman's patient was weakly and had always suffered from dyspnœa. Death took place at 19, after seven and a half months of failing compensation. Lebert's patient, aged twenty-two years, had long had epistaxis and dyspnœa, and developed cardiac symptoms in the last two years.

Physical Signs.—These bear no constant relation to the symptoms, but may be present where these are quite lacking. Nor, on the other hand, do they correspond to the degree of the constriction, nor to the extent of the collateral circulation, both of which may be developed to an extreme degree without yielding any evidence of their presence.

The most marked signs appear to be produced in association with chronic valvular disease or bicuspid aortic valves, or with the relative mitral incompetency of the later stages of the cardiac dilatation that frequently supervenes, in which cases the murmurs formed in the heart may be propagated along the vessels. The signs peculiar to the lesion may best be studied in uncomplicated cases. They are both vascular and cardiac, and are present in varying degrees and combinations in the majority of cases.

Vascular.—These depend chiefly upon the inequality of the circulation in the upper and lower halves of the body, and upon the unusual appearances presented by the dilated collaterals. In well-marked cases the vessels of the upper half of the trunk may be seen pulsating, the subclavians, as a rule, more markedly than the carotids; and pulsation may be traced in many cases along the abnormally dilated and tortuous vessels occupying the course of the internal mammaries on either side of the sternum, or the posterior intercostal or scapular arteries behind. In Libman's patient there was a varicose mass beneath the skin of the abdomen; in Flint's, both supraspinous fossæ were occupied by a network of tortuous pulsating vessels; in Leudet's, small arterial dilatations extended over the middle of the thorax both in front and behind, and were most marked at the posterior border of the left axilla and in the left supraspinous fossa, where they formed tortuous, thickened vessels, pulsating synchronously with the radials. Along the whole course of these a murmur, usually postsystolic in rhythm, but sometimes systolic or double, may be heard, and a slight thrill may be felt.

The radial pulse is frequently hard and full, and may be unequal on the two sides. The lower extremities may contrast strangely with the upper half of the body in the absence of all visible pulsations. On examination the pulse in the abdominal aorta and femorals is either very weak or absent, while the murmur usually audible on pressing over the femoral with the stethoscope cannot be heard. In Bonnet's case, diagnosed before death, no pulse could be felt in the abdominal aorta or femorals, and an artery pulsating visibly and as large as the radial, over which an intense systolic murmur could be heard, ran downward between the vertebral column and the inner border of the left scapula. On the right side of the column a similar but less strong pulsation could be felt, but no murmur was heard.

Hornung's patient, a man aged twenty-seven years, is an example of an extreme stenosis not producing any symptoms, but with marked physical signs, in whom death occurred suddenly from rupture of the aorta. There was energetic pulsation and a systolic murmur over the carotids and subclavians. At the inner border of the scapular region were sinuous pulsating vessels. The radial pulse was hard and resistant, and there was no pulsation in the abdominal aorta, popliteal, posterior tibial, or pedal arteries. As long ago as 1839, Mercier diagnosed a case in which there were visible pulsations in the intercostals, a marked bruit at the lower angle of the left scapula, and a very weak pulse in the lower extremities, with epistaxis and symptoms of failing compensation for three months before death.

Cardiac.—The heart's action may be tumultuous, with a heaving impulse, and the organ may present evidences of enlargement, particularly of the left ventricle. A precordial thrill was present in only 3 of the cases. The heart sounds may be quite pure, or accompanied by loud murmurs, usually systolic or postsystolic in rhythm. In Hornung's patient a rough murmur was heard at the aortic area, most marked between the left clavicle and the third rib. In Decker's, a woman aged nineteen years, with complete obliteration at the isthmus and no complicating valvular disease, a rasping murmur filling the whole systole was heard at the apex, and could also be traced along the thickened, tortuous, and dilated arteries, among which the superior epigastric, the long thoracic, and the dorsalis scapulæ formed pulsating cords; the heart was hypertrophied.

Diagnosis.—When such symptoms and signs as the above occur together a very distinctive clinical picture may be formed. It must be remembered that they may be entirely absent, or present only in a fragmentary way, such as may awaken suspicion of the reality, yet render a positive diagnosis impossible. The fact that physical signs as well as symptoms usually do not remain stationary, but progress to a more definite development, furnishes the clue by which the presence of the anomaly may best be traced. A pulsation at an abnormal area, or a superficial murmur of unusual site, noted and watched, may lead to a second examination, at which the full development of the condition may be revealed.

Even where symptoms are present, the diagnosis may be very difficult between a constriction of the descending aorta at the isthmus and obstruction of this vessel or its branches by aneurism, or by the pressure of a mediastinal tumor. The absence of any considerable area of dulness, the transmission of the murmur for long distances along the branches of the ascending arch, the remarkable extent to which the collateral circulation is sometimes developed, above all, the results of *x*-ray examination, contribute differential points in favor of coarctation. In perhaps no other pathological condition are more extensive changes compatible with fewer evidences during life. The later stage of cases in which vascular phenomena are lacking and failing compensation develops, may be impossible to distinguish from that of organic insufficiency of the mitral valve.

Termination.—The cases may be divided into three groups: (1) The condition may be latent throughout life and not interfere with its duration in any way. (2) Both in latent cases and in those presenting symptoms during life death may occur suddenly, by asystole, from rupture of the heart or aorta, or from causes unknown. (3) Death may follow a stage of broken compensation, which may be preceded by symptoms characteristic of the lesion, or may develop suddenly in an apparently healthy subject.

HYPOPLASIA OF THE AORTA AND ITS BRANCHES.

Hypoplasia of the aortic system may be described as that condition in which the lumen of the arterial vessels in the greater circulation remains abnormally small and the walls unnaturally thin and elastic. The heart

may also be reduced in size or may undergo a compensatory dilatation and hypertrophy which involves especially the left ventricle, but may extend to the whole organ, and is usually succeeded by a marked degree of secondary dilatation. The subjects are, as a rule, pale individuals of delicate frame, who present signs of retarded development, such as a delayed advent of the signs of puberty. Anomalies of the sexual organs frequently occur. The general health is usually fair until early adolescence, when the condition generally manifests itself after some unusual physical strain has been endured, by the sudden appearance of failing compensation. The course is then progressively downward. In women, who are by natural conditions less exposed to undue muscular exertion than are men, this stage of cardiac insufficiency may not supervene, but the disease may run its course under the guise of a chlorosis. By some observers (Ortner, Hiller) the narrowing of the vessels is thought to predispose to the infectious fevers, and a special group of cases in which death has occurred from typhoid fever is described. It is also seen in young anemic subjects dying of pulmonary tuberculosis.

There has been some debate as to the pathological significance of the condition. Several authors have maintained that the greater elasticity of the walls of the vessels compensates for their smaller calibre, and so prevents undue strain upon the heart. A number of statistical contributions, have, however, demonstrated that hypoplasia of the aorta must be given a place in pathogenesis as one of the special causes of cardiac asystole. The *etiology* is obscure. In some few cases, such as the cachexias of wasting diseases, a true atrophy of the aorta occurs. In the majority some congenital defect, amounting in some instances to a congenital tendency to dwarfism, may be supposed. This view is supported by the frequent association of other anomalies, especially in the generative and circulatory systems.

Typical cases were described by Morgagni in 1761 and by Meckel in 1788. Rokitsky defined the condition in 1838 and commented upon its association in some instances with defects of the external genitalia. Bamberger, in 1843, noted the association of chlorosis with a small aorta. But in general the subject attracted little attention until Virchow, in 1872, published a series of cases illustrating the frequency of a small elastic aorta and a small heart in chlorosis, and suggested an etiological relation between the two conditions. He explained the absence of compensatory hypertrophy of the heart in some cases and its presence in others, as depending upon the degree of diminution of the lumen of the vessels, the volume of the circulating blood, the elasticity of the vessel wall, and the amount of work done by the individual. Ortner, in 1891, dwelt chiefly on the medicolegal aspect of the subject, and emphasized as pathognomonic an absence of the jugular pulsation in the episternal notch in cases in which the upper border of the cardiac dulness is high. Spitzer (1897) attempted by a study of the recorded material to place the condition on a more definite clinical basis. He pointed out that while the cases usually terminate with failing compensation, this resembles the end stages of chronic valvular disease only in a general way, that the symptoms are in general those of a cardiac overstrain due to

muscular fatigue, and have a progressive tendency to grow worse; that during the stage of broken compensation the cardiac dulness is usually much enlarged, and that the sounds are generally clear, with marked pulmonary accentuation, although occasionally accompanied by murmurs. Like Virchow, he noted as characteristic a remarkable *pallor*, but he ascribed it not to a diminution of the hemoglobin, which he found usually 90 to 100 per cent., but to the reduction in size of the vessels through which a smaller quantity of blood coursed beneath the skin.

Burke¹ (1901) gave a historical review of the subject and a full account of all the cases on record. He divided the material into four groups:

(1) Hypoplasia of the aorta in the so-called blood diseases, as chlorosis, pernicious anemia, hemophilia; (2) hypoplasia in association with infectious diseases, considered as predisposing to these or tending to their fatal termination; (3) hypoplasia with general dystrophies, as acromegaly; (4) hypoplasia presenting the picture of a cardiac lesion, the mass of the cases belonging to this last group. Apelt² collected 100 cases from the literature and added an account of two cases, both of which were diagnosed during life. The subjects were young men aged seventeen and twenty-one years, of slight build and medium size, who had been capable of the usual amount of physical exertion, and had presented no symptom of disease. Both passed through a period of unusual physical strain just before the sudden onset of symptoms, which took place a few weeks before death. The picture was that of an acute dilatation of the heart with slight terminal cyanosis, œdema, ascites, the cardiac area enormously increased, and the pulmonary second sound markedly accentuated. The heart sounds were pure except toward the close in one patient, in whom a systolic mitral murmur developed. Postmortem, in both cases, the arteries were throughout thin, delicate, elastic, and of diminished calibre, and there was moderate hypertrophy with great pathological dilatation of the heart, although its valves and chordæ tendineæ were delicate, and healthy. Microscopic examination revealed an entire absence of fatty degeneration of the myocardium.

Van Ritoök analyzed 73 cases, 56 from the literature including the series of Burke and Apelt, and 17 from personal observation, and he enumerated the following points as of diagnostic value: (1) The youth of the patient. (2) Marked and obstinate anemia persisting in spite of all treatment. (3) The early development of fatigue in a young individual on slight physical exertion. (4) Subnormal temperature or only slight rise of temperature in febrile diseases. (5) Palpitation. (6) Hypertrophy of the left heart. (7) Acute cardiac insufficiency developing after comparatively slight physical strain. (8) Diminished resistance to infectious diseases.

ANOMALIES OF THE AORTIC ARCH.

Quite a wide variation of anomalous conditions of the aortic arch and its branches occur, the individual forms of which repeat themselves

¹ *Deut. Arch. f. klin. Med.*, 1901, No. 71, 187.

² *Deut. med. Woch.*, 1903, xxxi, 1186.

in different subjects with such similarity, that an underlying developmental error may be inferred. The units of the series may be summed up under the various headings of (1) double aortic arch, (2) right aortic arch, (3) origin of left subclavian artery, from (*a*) a patent ductus arteriosus, or (*b*) the pulmonary artery, (4) origin of the right subclavian artery from the descending thoracic aorta below the left subclavian artery, and (5) common brachiocephalic trunk. In all these the underlying defect is either a persistence of an embryonic arch which normally undergoes involution (double aortic arch, right aortic arch, left subclavian from patent ductus), or an arrested development of a portion of the embryonic arches that normally persists (right subclavian from thoracic aorta, common brachiocephalic trunk). In man the primitive aorta is at first double and of the six embryonic arches the first, second, and fifth disappear on both sides as well as the left sixth and the distal part of the left fourth, while the third parts persist as the carotid arteries, the fourth left as the aorta, the proximal portion of the right fourth, as the subclavian, and the left sixth becomes the pulmonary artery with the ductus arteriosus.

Double Aortic Arch.—In this anomaly, of which some 8 cases have been recorded, the aorta ascends to the right and turns backward and divides near the beginning of its transverse portion into two large trunks which lie parallel with each other and unite just beyond the insertion of the ductus to form the descending arch, enclosing between them an elliptical space in which the œsophagus and trachea lie embraced within the vascular circle thus produced. The posterior member of the pair, which is usually the larger, appearing as the true arch of the aorta, gives off the right carotid and subclavian, and lies behind the trachea. The smaller anterior limb lies below the other, appearing like a loop from it, and gives off the left carotid and subclavian, either as a simple trunk (left innominate) or as separate vessels. Examples are the cases recorded by Curnow¹ in a woman, aged eighty-seven years, and by Hamdi,² in a woman aged forty-five years. In the latter case the trachea and œsophagus were slightly compressed. Although no symptoms had been produced, the deformity of the trachea was sufficient to prove the possibility of a fatal obstruction.

Henle explains the posterior limb of the double aorta as a persistence of the fourth right arch. The anterior limb represents the fourth left arch, and the two unite at the point of insertion of the ductus (sixth arch) to form the descending aorta as in the embryo, and as is persistent in the amphibia.

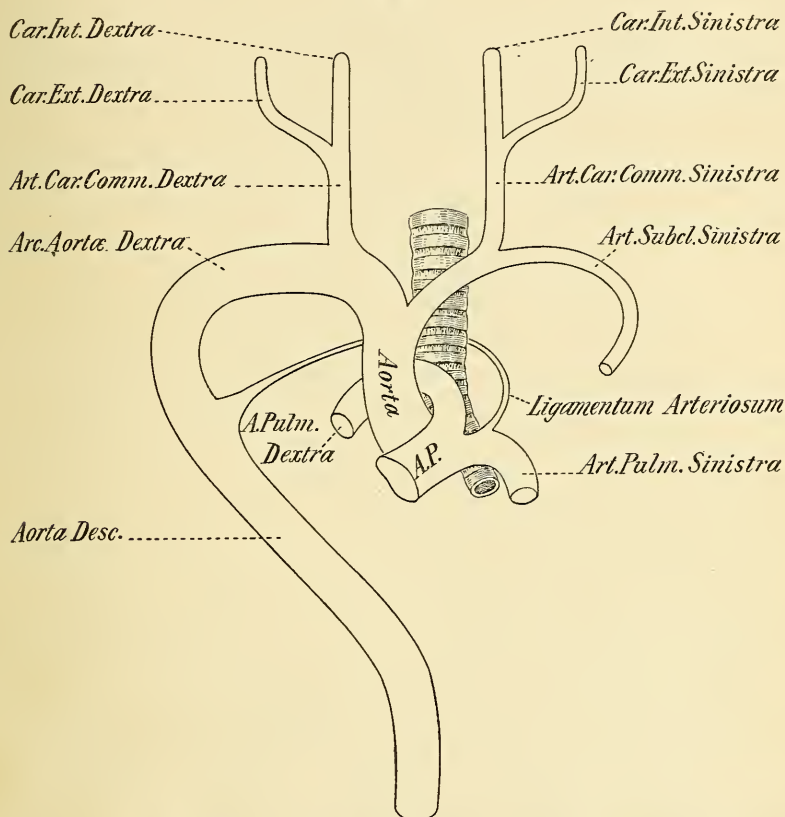
Right Aortic Arch.—In this anomaly the aorta is normal at its origin, but curves over the root of the left instead of the right lung, so that its *convexity* lies to the *left*, and it passes down on the right side of the aorta, the right recurrent laryngeal nerve hooking round the arch in the same manner as does the left under normal conditions. The left carotid, or, in some cases, a left innominate artery, arises from the front of the aorta shortly after its origin and represents the persistent *left*

¹ *Trans. Path. Soc.*, London, 1874, xxvi, 23.

² *Deut. med. Woch.*, 1906, xxxii, 1410.

aortic root. The right carotid rises next in about its normal situation, and then the right subclavian more posteriorly and to the right, while the left subclavian arises either (a) in its normal situation or (b) with the left carotid from the left innominate, or from a patent ductus or from the pulmonary artery.

FIG. 41



Dr. Kaufmann's case of right aortic arch with ligamentum arteriosum encircling the trachea and oesophagus. Diagrammatic representation following Evans' diagram of the survival of the aortic arches, to show that in the present case the fourth right arch (represented by the arch and trunk of the descending thoracic aorta), the left proximal part of the fourth left arch (represented by the left innominate and subclavian), and the left sixth arch (represented by the ligamentum arteriosum), survive, and that the trachea is necessarily encircled by the passing over of the ductus to the arch of the opposite side. The oesophagus is here omitted for the sake of clearness: *Car. Int. Sinistra*, left internal carotid; *Car. Ext. Sinistra*, left external carotid; *Art. Car. Comm. Sinistra*, left common carotid; *Car. Int. Dextra*, right internal carotid; *Car. Ext. Dextra*, right external carotid; *Art. Car. Comm. Dextra*, right common carotid; *Art. Subcl. Sinistra*, left subclavian; *Art. Subcl. Dextra*, right subclavian; *Arc. Aortic Dextra*, right aortic arch; *Art. Pulm. Sinistra and Dextra*, left and right pulmonary arteries; *D. A.*, funnel-shaped patent aortic end of ductus; *A. P.*, pulmonary artery. (Drawing by Prof. G. Adami, McGill University.)

The curve of the aorta passing from the right to left and then back to the right side of the vertebral column becomes very sinuous in those cases in which the ligamentum arteriosum or a patent ductus remains attached to the right aortic arch at its usual site of insertion opposite

or near the left subclavian. In these cases the ductus is forced to pass from its origin in the pulmonary artery, on the left side anteriorly, backward and to the right to meet the right arch which curves toward it *behind* the trachea and œsophagus which are thus again, as in double aortic arch, engaged in a complete vascular circle formed in this case by the aorta, ductus arteriosus (patent or obliterated), and the pulmonary artery. Four such cases are recorded, in two of which the ductus was obliterated; in the third, it was widely patent, and in the fourth case (a specimen in the McGill Museum presented by Dr. Kaufmann, which has been figured for me diagrammatically by Professor Adami, see Fig. 41), it was widely patent at its aortic end, but was closed beyond, the ligamentum arteriosum forming a long thick cord. In the latter case the aorta gave off a left innominate trunk and then curved backward soon after its origin and to the left, passing behind the trachea and œsophagus and gaining the right side of the vertebral column below. At the point where the convexity of the arch gains the left side of the trachea, it presents a deep triangular pouch, which represents the patent aortic end of the ductus, to the apex of which externally a cordlike structure of remarkable length and thickness, the ligamentum arteriosum, is attached. This ligament passed forward anteriorly to the trachea and œsophagus to its attachment in the left branch of the pulmonary artery, and encloses these viscera within the vascular circle formed by it with the aorta and pulmonary artery.

Such cases form a link between simple right aortic arch, in which the aorta lies entirely on the right side of the trachea, and double aortic arch in which trachea and œsophagus are completely embraced by a vascular ring. They throw light on the development of the latter, at first sight inexplicable, phenomenon. For, since a right aortic arch must pass behind the trachea to unite with the persistent sixth left arch which is represented by the ductus, it must do the same to unite with persistent left fourth arch which is represented by the anterior limb of the double pair. The whole situation is explained by the reflection that in the embryo these viscera occupy a position, not behind, but on the left posterior aspect of the primitive heart, and that the pairs of embryonic arches pass on either side of them to their destination in the dorsal aorta, so that if arches on opposite sides unite as they have done in the anomalies under consideration, trachea and œsophagus are bound to be encircled.

Left Subclavian from Ductus Arteriosus or Pulmonary Artery.—While the left subclavian is given off from the fourth right aortic arch, it is practically a continuation of the distal part of the sixth left arch represented by the ductus arteriosus to which its origin bears a constant relation.

Right Subclavian from Descending Thoracic Aorta.—In this anomaly the aortic arch has its normal course to the left, but the right subclavian is given off from a point in the thoracic aorta just below the insertion of the ductus arteriosus and passes up to its normal distribution. Here an arrest of the proximal part of the fourth right arch which normally forms the right subclavian has occurred, and the obliteration

of the distal portion which in the embryo unites the fourth arch with the aortic trunk has not taken place.

Common Brachiocephalic Trunk.—All four great vessels may arise by common origin, recalling the embryonic stage in which all the arches emerged together from the third carotid arch. A case is cited by Freyberger.¹

Clinical Aspects.—The evidences presented during life and the clinical significance of all the above conditions are slight. In right aortic arch and common brachiocephalic trunk the aorta is apt to rise higher toward the neck than is normal, leading to violent pulsation in the episternal notch, which may lead to a mistaken diagnosis of aneurism. In the case of origin of the left subclavian from the pulmonary artery or patent ductus the left arm usually remains entirely free from cyanosis, which shows how far the system can accommodate itself under favorable conditions to an admixture of venous with arterial blood.

ANOMALIES OF THE CORONARY ARTERIES.

Anomalous Origin from the Pulmonary Artery.—A vessel may arise from a sinus of Valsalva of the pulmonary artery, and, meeting the branches from the aortic coronaries, produce a remarkable anastomosis of a cirroid character. In Brook's first case, a vessel the size of a crow-quill sprang from the right anterior sinus of Valsalva of the pulmonary and passed down over the infundibulum of the right ventricle, there anastomosing with the aortic coronaries. In his second case a large anomalous artery arose from the same situation. It gave no branches to the heart but passed to the left and upward to enter a complicated mass of thin-walled arteries, which lay around the main pulmonary trunk and passed up along the trachea and behind the aortic arch. This mass received three other large vessels, one from the left subclavian, one from the right aortic coronary, and one from the posterior aspect of the transverse aortic arch. Krause's case is similar.

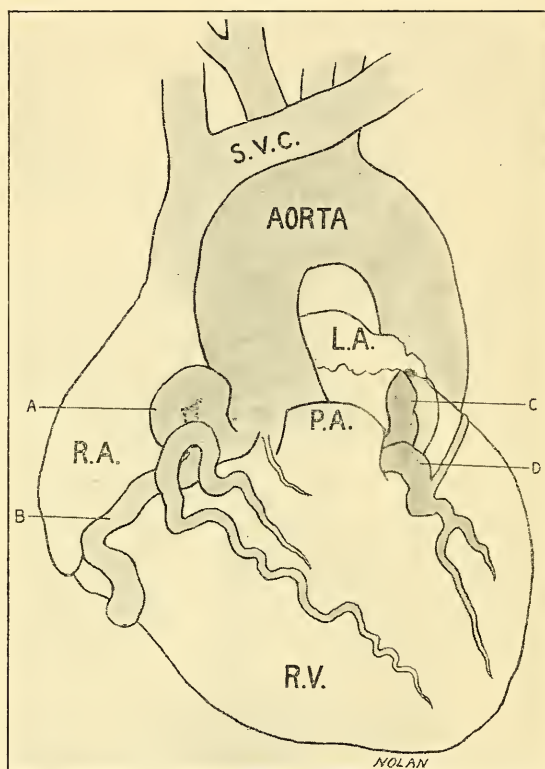
The McGill specimen (see Fig. 42), was from a woman aged sixty years, who died accidentally. The right coronary arose in its normal situation from the anterior sinus of Valsalva of the aorta by a much dilated orifice, and expanded directly after its origin into a huge thick-walled loop the size of a crab-apple, which projected upward some 2.5 cm. above the subepicardial fat, and gave off the descending branches from the loop. Both these and the main trunk of the vessel were wide, thick-walled, tortuous channels. No coronary arose behind the left posterior aortic cusp in the normal situation of the left coronary, but instead a large patulous opening lay in the floor of the dilated posterior sinus of Valsalva of the pulmonary artery. From this sprang a large thin-walled trunk of venous character, which divided about 1 cm. beyond its origin into two large branches, one of which ran to the left in the auriculoventricular groove in the course normally followed by the transverse circumflex branch of the left coronary artery, while the

¹ *Trans. Path. Soc.*, London, 1898, xliv, 44.

² *Jour. Anat. and Physiol.*, 1902-03, xxvii, 387.

other ran downward along the front of the interventricular septum in the position of its descending branch, and was here expanded into a large triangularly shaped venous sinus, 2 cm. in its widest diameter, and diminishing in size toward the apex. In the floor of this sinus were several thick-walled septa behind which large vessels opened into it from the myocardium.

FIG. 42



Aneurismal dilatation (arteriovenous aneurism) of branches of coronary arteries in a case of anomalous origin of the left coronary from the pulmonary artery. (From a specimen in the Medical Museum of McGill University, Montreal.)

The question of the circulation in the anastomosing vessels, in which blood from the systemic and pulmonary circulations must have mingled is of interest. Brooks suggests that the direction of the current must have been *toward* the cirroid aneurism in the coronaries arising from the aorta, and toward the right ventricle in the coronary that arose from the pulmonary artery, which would thus drain the mass and would also send some arterial blood to the lungs.

In the McGill specimen the peculiar septa in the floor of the large venous sinus formed by the descending branch of the anomalous vessel, strongly suggested that the course of the blood was *toward* the pulmonary artery. This case is additionally interesting from the fact that the anomalous vessel was here clearly the left coronary, which was absent

from its normal situation and arose from the pulmonary. Both this and Brooks' second case were in elderly subjects, and the condition had not produced any manifestations during life.

Miscellaneous Anomalies.—Accessory coronaries may be present or both vessels may arise behind a single aortic cusp, or there may be a complete absence of one. A case has been recorded of an anomalous coronary sent to the lungs in pulmonary atresia.

ANOMALIES OF THE PULMONARY ARTERIES.

Accessory Pulmonary Artery.—A series of 10 cases has been collected from the literature by McCotter,¹ in which an anomalous artery had arisen from the aorta or its branches, and had supplied the lower lobe or the accessory lobe of one or other lung. In the case reported by himself, in a man aged sixty-five years, this artery was 7 mm. in diameter, and was given off from the front of the thoracic aorta on a level with the tenth dorsal vertebra, and passed up to the right between the folds of the ligamentum latum pulmonis to the lower margin of the right lung, where it ramified. The lung pleura and mediastinum were otherwise normal. In 8 of the cases collected the accessory branch was from the thoracic aorta, in one from the abdominal aorta, and in one from the seventh intercostal artery. In 5 cases the accessory branches supplied an accessory lobe and in 5 the lung was normal.

Pathogenesis.—The final explanation must be deferred until the origin of the pulmonary circulation is better understood. McCotter gives an interesting discussion. Accessory pulmonary arteries have been described in amphibia and reptiles, and are said to be normal in the latter. Thoma and Evans found that the blood vascular system in the embryo arises as a capillary plexus spreading in all directions. Such a capillary plexus forms caudally from the pulmonary arches and envelops the primitive lung *anlage* with a rich capillary plexus. In the case of the accessory pulmonary branch, this plexus must have formed laterally from a primitive thoracic aorta and joined the pulmonary plexus just as a capillary network extends to the limb-bud. The explanation of this anomaly is thus either (1) that this plexus always occurs but has failed to atrophy in the present case; or (2) that the plexus is only occasionally laid down, *i. e.*, is in itself an anomaly, and when present results in an accessory pulmonary branch. The condition has not shown itself to be of any clinical significance.

ANOMALIES OF THE SYSTEMIC VEINS ENTERING THE HEART AND OF THE PULMONARY VEINS.

Systemic Veins.—*Persistent left superior vena cava* is the commonest of these anomalies. It is not infrequent in conjunction with other cardiac defects, and occurred 26 times in our series. It is of little clinical

¹ *Anal. Rec.*, August, 1910, 291.

importance but is of great interest in cases where the congenital origin of the associated condition is questioned, as indicating the developmental nature of the latter. The cases may be divided into two groups: those in which the right superior cava is also present, and those in which it is absent, and the blood from the upper portion of the body enters the right auricle through the persistent left cava. A series of 4 cases of persistent left cava is published by Schutz.¹ In three of these the right cava was also present, in one it was equal in size to the left; in a second it was small and the left cava communicated with the left auricle by a valvular opening in its wall before entering the right auricle at the coronary sinus. In this case the apex of the heart was bifid; and the patient was a woman of thirty-eight of whom no other history was obtainable. In the third case the left superior cava was persistent but rudimentary. In Schutz's fourth case the *right superior cava was absent*. The left innominate veins emptied into the left innominate at the level of the left common carotid to form a left superior cava thicker than a man's thumb which widened into a bulbar swelling 4.5 cm. across, which entered the coronary sulcus and opened into the right auricle above the inferior vena cava. Habershon² reported a case of absence of the superior cava in a man aged thirty-seven years. The usual opening of the superior cava in the right auricle was marked by a smooth, white area of endocardium, like a closed foramen ovale, and there was extensive development of collateral circulation through the vena azygos major. The persistent left cava was formed by a union of the left jugular and subclavian and right innominate veins and emptied into the dilated coronary sinus. The recent literature on complete absence of the right superior cava with persistent left is given by Dietrich.³

A very interesting case is published by Beyerlein,⁴ in a boy, aged one and a quarter years, of double superior vena cava, in which the orifice of the coronary sinus in the right auricle was obliterated by the overgrowth of an extensive network of Chiari. The persistent left cava received all the blood from the coronary veins and the heart, and emerged from the coronary sulcus at the normal situation, emptying into the right superior cava through the transverse branch. Two cases practically identical with this very rare anomaly are reported by Gruber⁵ and LeCat (quoted by Gruber). Nabarro⁶ describes a case of double superior cava in an infant of three months where the persistent left duct, smaller than the right, was joined by the left hepatic vein, which emptied with it into the coronary sinus. Here the left horn of the embryonic sinus venosus had evidently escaped obliteration.

A series of cases in which a *displacement to the left* of the superior cava has taken place so that its orifice comes to lie directly above the interauricular septum, and looks into both auricles, which has been

¹ *Virchows Arch.*, 1914, ccxvi, 35.

² *Trans. Path. Soc.*, Lond., 1876, xxvii, 79.

³ *Virchows Arch.*, 1913, ccxii.

⁴ *Frank. Zeit. f. Path.*, 1914, xv, 327.

⁵ *Virchows Arch.*, 1885, xcix, 492.

⁶ *Jour. Anat. and Path.*, 1902, xxxvii, 387.

described by Ingalls and others, and a similar condition of the inferior cava by Rokitansky, are described under auricular septal defects.

Pulmonary Veins.—An anomalous distribution of the pulmonary veins is much more common than is generally supposed, and quite serious deviations from the normal have been attended with surprisingly little results. Nevertheless, their displacement occurs in many complicated anomalies, and their repeated combination with these grave defects suggests a primary error in development in the pulmonary veins *anlage*. Quite a large series of cases of biloculate heart are reported in which the pulmonary veins were deflected from their entrance to the left auricle and were received by one or other of the great veins. Schroeder¹ gives a full discussion of the various anomalies of the pulmonary and systemic veins and traces their developmental origin, with especial reference to those cases, like his own, in which a complete defect of the interauricular septum was associated. Nabarro describes the pulmonary veins opening into the coronary sinus in an infant aged five and a half months, in whom all the blood from the systemic circulation must have passed through the patent foramen ovale.

In the cases reported by Ingalls,² Chiari and others, of defects at the upper part of the interauricular septum, the right pulmonary veins either entered the right auricle or the superior vena cava. In those reported by Borst and Stoeber³ of an anomalous septum in the left auricle, the pulmonary veins entered the smaller upper chamber in the left auricle to the right of the anomalous septum, which evidently represented the septum primum, deflected to the left by the entrance of the pulmonary veins too far to the right side. In all, the primary defect is apparently the deflection of the pulmonary veins.

Ramsbotham describes a case in which the left pulmonary entered the left subclavian, and the right pulmonary the portal vein, and in three others (Arnold, Bochdalek, Geipel) the right and left pulmonaries entered the portal vein together as a common trunk. The pulmonary veins of both sides may enter the left auricle as a single or as two trunks. Here the original single vein has not been taken up in the wall of the auricle as occurs in normal development.

The *clinical significance* of these conditions depends less upon the defect itself than upon the associated developmental conditions.

DIAGNOSIS, PROGNOSIS, AND TREATMENT OF CONGENITAL CARDIAC DISEASES.

Differential Diagnosis.—In the diagnosis of congenital cardiac disease two questions are to be considered: a congenital is to be distinguished from an acquired lesion, and the differentiation may be attempted of the particular defect. The first of these is the more important as well as the simpler problem. It is necessary both for a wise prognosis and for proper treatment to recognize the congenital nature of the lesion,

¹ *Arch. für. klin. Med.*, 1911, ccv, 122.

² *Johns Hopkins Hosp. Bull.*, 1907, xviii, 136.

³ *Virchows Arch.*, 1908, cxliii, 252.

and this can usually readily be done. The following conditions are significant of the presence of a defect: (a) The youth of the patient. (b) A history of symptoms originating in early childhood or in infancy, and of the absence of any event, as rheumatism or endocarditis, which could have led to an acquired lesion. (c) The cyanosis when this is present, and the symptom complex associated with it. (d) The presence of atypical physical signs.

The diagnosis of the various defects from each other is a more difficult task. In some of the most complicated forms of congenital cardiac disease both signs and symptoms may be conspicuous by their absence. And on the other hand, several anomalies are frequently combined in the same case, so that a bizarre picture is liable to be produced, even in the presence of marked physical signs. Nevertheless, a careful study of the literature, and the application of this at the bedside has convinced the writer that in the great majority of cases auricular and ventricular septal defects, abnormal communication between the aorta and pulmonary artery, patent ductus arteriosus, subaortic stenosis, and coarctation of the aorta, all of which conditions are characterized usually by *slight* or *absent cyanosis*, can be distinguished from each other and from pulmonary stenosis or atresia, and from those forms of biloculate and triloculate heart, persistent truncus arteriosus and transposition of the arterial trunks, *in which the cyanosis is a more conspicuous feature*. This statement has the authority of Hochsinger, whose special work along the line of congenital defects convinced him that the differentiation of cardiac defects is largely a question of familiarity with the clinical features.

Cyanosis is the rule (to which a few exceptions occur) in pulmonary stenosis and atresia, in complete defects of the septa, as biloculate or triloculate heart or persistent truncus arteriosus, and in transposition of the arterial trunks. It is frequently absent, but may be present and this especially as a terminal event, in patent foramen ovale and in defects of the interauricular and interventricular septa. Cyanosis is usually *absent*, except during dyspnoëic attacks, in patent ductus and in coarctation and hypoplasia of the aorta.

Dyspnœa, though always present to a certain degree when cyanosis is advanced, does not appear to bear a definite relation to the degree of deficient aëration but evidently depends on some other factor as well. It is thus characteristic of many cases, such as patent ductus, patent foramen ovale, or septal defects, in which no trace of cyanosis is seen, shortness of breath and palpitation on exertion from early childhood, being quite frequently complained of. The same is true of *dyspnoëic suffocative attacks* with transient cyanosis which form an important diagnostic feature of such cases.

The distinctive character of the *physical signs* in those defects which are of clinical significance have been discussed under the individual lesions but may be briefly summarized. A harsh, *systolic murmur* and thrill localized over the upper part of the precordium and of diminished intensity or inaudible at the apex is characteristic of pulmonary stenosis and of septal defects. It may in a few cases be heard best at the apex,

and it may vary in rhythm, particularly in septal defects. Both in pulmonary stenosis and in patency of the duct the murmur usually has its maximum intensity high up over the second left interspace and may be heard beneath the left clavicle. That of the auricular and ventricular septal defects is heard over the third and fourth left interspaces. Murmurs of congenital lesions, when heard in the back, are usually due to patency of the duct or to septal defects. A precordial *thrill* with the same localization as the murmur is present in about 15 per cent. of congenital defects with physical signs, its presence as a rule corresponding to the degree of harshness of the accompanying murmurs.

In *defects* of the *interauricular septum* the murmur is often post-diastolic or presystolic, and in patent foramen ovale presystolic and systolic murmurs may combine or alternate with each other, and may vary with change of position, their inconstancy supplying a differential point.

In *patent ductus*, a harsh rumbling machinery murmur, beginning toward the close of systole and continuous throughout the cardiac cycle is present in a certain number of cases, and when it occurs is pathognomonic; in others the murmur is systolic or (rarely) diastolic. The pulmonary second sound is here usually accentuated and helps to differentiate patent ductus from pulmonary stenosis, in which the pulmonary second is usually (not always) weak or absent. An abnormal area of dulness above and distinct from the cardiac dulness, in the first and second left interspaces (Gerhardt's sign), is also significant of the latter stages of patent ductus, as indicating a dilated pulmonary artery. This sign may be produced also by retraction of an atelectatic left lung (Hochhaus), so is not positive unless confirmed by the *x*-rays.

A powerful *diastolic* murmur and thrill with maximum intensity over the second and third interspaces, and an accentuated second pulmonary sound characterized several of the cases of abnormal communication between the lower part of the aorta and pulmonary artery (defect of the aortic septum) recorded.

Complete *transposition* of the arterial trunks has been diagnosed by the absence of physical signs in the presence of marked cyanosis, and an accentuated pulmonary second sound (Hochsinger).

Coarctation of the aorta is to be recognized by the evidences of the collateral circulation when this has been established, hypertrophy of the left heart, the frequent association of an acquired aortic insufficiency, and a reduction in the force of pulsations in the lower extremities as compared with the upper.

The above are a few of the indications by which typical cases may be distinguished from each other. But in this subject it should be remembered that hard and fast lines may not be drawn. Thus rhythm, maximum intensity, transmission of murmur or thrill, and all other manifestations of the defect will be found to vary with the associated cardiac conditions, valvular and myocardial, congenital and acquired, far more here, where so wide a range of combinations is possible, than in the acquired forms of heart disease. For this reason we look with interest to the introduction of the newer methods of precision in this difficult

and little studied field. Several positive findings have already been recognized and are indicated below. There is good reason to believe that their further application will supply us with a more exact knowledge upon the differential diagnosis of congenital defects.

Graphic Methods.—*X-ray Examination and Orthodiagraphic Tracings.*—Definite information upon the existence of hypertrophy of the ventricles and dilatation of the auricles is to be obtained from the skiagraph. Examination of the shadow at the base of the heart shows also a distinct widening in the presence of dilatation of one or other of the great trunks. When the pulmonary artery is the one dilated the widening appears as a distinct bulging on the left side just above the upper border of the heart, forming an “x-ray cap” in the position of the so-called Gerhardt’s dulness. Dilatation of the aorta is indicated by an increased shadow to the right of the median line in the same situation. Conversely, hypoplasia of the pulmonary artery is indicated by a narrowing of the shadow to the left of the heart’s base. These points and the typical shape which the ventricular portion of the heart assumes in the various valvular lesions are well shown in the heart-silhouette obtained by the orthodiagraphic tracing. Groedel¹ has figured the outline obtained both in the various acquired valvular lesions and also in congenital pulmonary stenosis, patent ductus arteriosus, and coarctation of the aorta and points out that in patent foramen ovale and in ventricular septal defects there is no change observed at the site of the great vessels so that unless hypertrophy of the ventricles has occurred the silhouette is normal.

Fluoroscopic Findings.—Deneke² diagnosed a case of interventricular septal defect in transposition of the arterial trunks by the appearance on fluoroscopic examination. The heart showed a moderate degree of hypertrophy of the right ventricle, and this chamber formed the right border of the heart in place of the right auricle as normally occurs, so that the strong pumping movement of the ventricle could be seen on the *right* border as well as on the left, instead of the fluttering auricular movement normally seen in this situation. Deneke describes the appearances as follows: “In normal hearts the movement of the right border is seen on the fluoroscope as a sharp auricular twitching preceding the contraction of the left. Its character can be readily distinguished as auricular, *i. e.*, a short fluttering contraction followed by long, passive dilatation. The movement on the left border is slow, lasting much longer than that of the auricular, and is a strong pumping motion followed by a short delay in the contracted state, then a gradual dilatation which is slower than the ventricular contraction, but much quicker than the dilatation of the auricles.”

The Electrocardiographic Curve in congenital hearts has been studied by Lewis,³ Owen,⁴ Nicolai,⁵ Ratner,⁶ Groedel and Mönckeberg,⁷ and

¹ *Deut. Arch. f. klin. Med.*, 1911, ciii.

² *Ibid.*, 1906, lxxix, 38.

³ *Clinical Electrocardiography*, 1913.

⁴ *Berlin, klin. Wchnsch.*, 1911, xlviii, 51.

⁵ *Cent. f. Herz. u. Gef. Leid.*, January 1, 1913.

⁶ *Heart*, iii, 113.

⁷ *Berlin Thesis*, 1912.

others. So far only a few positive points have been elicited, but these are sufficient to indicate the value of the cardiogram in this connection. (1) A "*negative initial Schwankung*" representing a deep exaggeration of the *S* wave, in lead *I*, has been observed in many congenital cases, and was described by Nicolai and Steriopulo as pathognomonic of cardiac defects. It is merely significant, however, of the extreme right-sided hypertrophy so common in these cases in which both right auricle and ventricle are involved, and is seen also in acquired mitral stenosis where the same condition of marked right-sided hypertrophy and dilatation occurs; as a corroborative sign it is often of use. (2) *An extreme amplitude of curves in several leads* was observed by Lewis in congenital cyanosis and is described by him as a "valuable sign of congenital valve or septal defects." (3) Finally, the electrocardiogram in true (mirror-picture) dextrocardia when the heart is transposed upon itself, supplies the most positive sign of this abnormality that we possess. In this case Lead *I* is completely reversed upon itself, and Lead *II* takes the place of Lead *III*, exactly the same tracing being obtained as when the leads themselves are reversed in a normal individual. The transposed electrocardiogram decides clearly between this condition and a simple dextroversio cordis. For a comparison of the electrocardiograms in these two conditions (see Fig. 22).

The *polygraphic tracing* may show a positive venous pulse of mitral insufficiency with communication between the two sides of the heart. In the absence of mitral stenosis (in which auricular fibrillation is so common and may give rise to this condition) and when other signs of tricuspid insufficiency are lacking this point may be of diagnostic value.

Estimation of the Oxygen Content of the Alveolar Air.—An important diagnostic point between those defects due to abnormal communications between the right and left sides of the heart, and those due to pulmonary obstruction has been supplied by Plesch,¹ working in Kraus' laboratory. In septal defects and patent ductus, there is usually an admixture of arterial blood with the venous current entering the lungs through the pulmonary artery, owing to the fact that under normal conditions the pressure in the aorta is greater, so that blood passes from left to right through the defects. Plesch estimated the amount of oxygen in the alveolar air expired from the lungs which he obtained by his method (described by Boothby and Peabody²), and found that in these conditions the venous blood passing to the lungs is reduced; that is to say, in terms of percentage of its oxygen content, the latter (O_2) is raised. This was also demonstrated in two cases of Vaquez disease (polycythemia with splenomegaly) in which the oxygen content of the alveolar air was examined by Senator-Lowy and v. Bergmann. On the other hand the alveolar air in cases of acquired valvular diseases and in one of congenital pulmonary stenosis was examined and showed no deviation from the normal. These figures and those showing the

¹ *Berlin. klin. Wchnschr.*, 1909, xlv, 392.

² *Arch. Int. Med.*, 1914, xiii, 502.

amount of oxygen consumed are shown in the table taken from an article by Kraus.¹

	Normal.	Polycythemia.			Congenital defects.			Mitral insufficiency.	Mitral stenosis.	Aortic insufficiency.
		Senator's case.	v. Bergmann's cases.		Persistent ductus arteriosus.	Septal defect.	Pulmonary stenosis.			
			I.	II.						
O ₂ used pro kilo and minute.	3.52	4.18	4.02	4.38	4.83 4.40	5.03	6.74	3.86	4.62	4.11
Reduction of venous blood in percentage of O ₂ content.	64	83	81	64	83 87	86	66	64	64	62

The differential diagnosis between the cyanosis and clubbing of congenital cardiac diseases and other forms is discussed under cyanosis.

Prognosis.—The duration of life has been considered in detail in connection with those defects that are of clinical interest, but a few generalizations may be made. The prognosis varies with the lesion and includes a wide range of possibilities, but is in general grave; this is based upon the direct interference with the circulation by the defect itself, and upon the well-known tendency of certain anomalies to become the seat of a future malignant endocarditis.

Among the least harmful forms of congenital cardiac disease may be mentioned anomalous septa in the auricles, patent ductus arteriosus, and coarctation of the aorta with extensive collateral circulation, which may exist until past middle life without symptoms, frequently terminating then with a general failure of compensation under some undue strain. Localized defects of the interauricular and interventricular septa belong likewise to the more innocent lesions which may give rise to symptoms, or may be present indefinitely without producing any effect upon the circulation, becoming serious only upon the advent of some pulmonary complication raising the pressure in the right heart, or through the engrafting of a malignant endocarditis along the edges of the defects.

In the more complicated defects life is correspondingly shorter. Young's patient with *cor biatriarum triloculare* and anomalous septum attained the age of thirty-nine years, and Holmes' twenty-four years, but these are rare exceptions, the subjects of biloculate and triloculate heart usually dying in infancy. This is true also of persistent truncus arteriosus, although a patient reaching twelve years is recorded by Crisp. In pulmonary stenosis early adult life is not uncommonly attained, but is rarely passed, the patients dying as often of tuberculosis as of the direct effects of the lesion. Here again in exceptional cases life may be prolonged, Vulpian recording pulmonary stenosis, *rechtslage* of the

¹ Chart from Kraus' article, *Berl. klin. Wchnschr.*, 1910, lxxiv, 230.

aorta, and defect of the septum in a man who died at the age of fifty-two years. The average duration of life in pulmonary stenosis is fifteen years, and in atresia 2.25 years in our series.

As graver conditions proving almost inevitably fatal during the first weeks or months of life may be enumerated: complete transposition of the arterial trunks without defect of the interventricular septum, pulmonary atresia with closed interventricular septum, tricuspid atresia, and aortic atresia, which is, indeed, the most serious of all, nearly all the cases recorded dying in the first two weeks of life, and many within a few hours of birth. The same is true of most forms of ectopia cordis. Finally, it is to be remembered that of the more complicated anomalies many must perish in the early stages of embryonic development, as only those in whom compensatory conditions arise survive until birth.

The prognosis depends largely upon the effects of the lesion upon the circulation, that is, upon the amount of deficient aëration produced, and upon the compensatory powers. For this reason symptoms will frequently prove a better guide to the immediate future than physical signs. Such conditions as septal defect, for instance, may give marked murmurs and thrill, yet lead to no hampering of the heart's action and to little interference with oxygenation until some additional factor, such as obstruction in the pulmonary circulation supervenes. Persistent cyanosis, a continued low temperature, a marked increase in the number of red blood cells (above 5,500,000), and dilatation of the heart, all point to a grave disturbance of the circulation and to a rapidly fatal issue. On the other hand, the entire absence of cyanosis and its attendant phenomena does not always argue a favorable prognosis, for in such cases sudden death may occur without any warning, either quietly, or in a paroxysm of cyanosis with dyspnoea. The embarrassment to the circulation which the lesion itself entails is not the only source of danger. Grave danger lies also in the frequent intercurrent of a malignant endocarditis, and in the fact that infections or bronchopneumonia are apt to prove rapidly fatal. The liability of patients with pulmonary stenosis to tuberculosis, and the frequent termination by sudden cerebral complications, are other unfavorable factors. These considerations indicate the extreme gravity of the more pronounced cases, and the fact that even in the more innocent forms of congenital cardiac disease the prognosis must be framed with reserve and caution. Among the better class, where good hygiene prevails and the most suitable conditions of living can be sought, the outlook is of course better than among the children of the very poor.

Treatment.—This may be said to begin with the care of the mother during her pregnancy, for a study of the etiology clearly shows that to some unhealthy condition in the environment of the embryo or in the parental organism, rather than to an ancestral tendency toward anomalous growth, the majority of cardiac anomalies owe their origin.

The treatment of a patient suffering from congenital cardiac disease must be largely symptomatic or palliative, or directed to the preventing of complications. The indications here are to do all that is possible to facilitate the oxygenation of the blood, to avoid additional taxation of

the burdened circulation, and to shield the patient from accidents or illnesses which increase the pulmonary or systemic obstruction, remembering always that in the majority cyanosis first develops on the addition of some such factor to the pathological conditions produced by the lesion itself. A carefully regulated life, a plentiful supply of light, fresh air, and warmth, the maintenance of an equable bodily temperature, the avoidance of mental agitation and of undue physical exertion, rest, and quiet forms of exercise, where this last is permitted by the condition of the patient, are all essential. The diet should be carefully ordered, light and nutritious, and the often capricious appetite watched. Free action of the excretory organs, especially of the skin, should be promoted and the child kept clothed with flannel. Sudden changes in the external temperature must be avoided and, when possible, resort should be had to a warmer winter climate. Exposure to cold or wet, or to any of the causes of rheumatism, should be avoided on account of the great liability to acute endocarditis. When adult life is attained, choice of light employment which does not call for sudden or great physical exertion is important. In women child-bearing is fraught with danger.

Operative interference in patent ductus arteriosus in the form of ligation of the duct, was suggested by Munro¹ on the ground that a probable diagnosis is now possible and that the vessel lies in an accessible situation. The fact that distinctive signs occur only after pulmonary dilatation has taken place and a certain adjustment of the vessels to the new order of the circulation has set in, would make one hesitate to resort to so radical a measure, which might introduce a new factor of disturbance.

When cyanosis has developed, the administration of oxygen has been suggested as likely to be useful in relieving dyspnoea. Gibson and others report a negative result from its use in several cases. For the relief of the dyspnoeic attacks diffusible stimulants are of benefit and should be kept at hand; and in infants the hot mustard bath is useful. The frequent syncope may best be relieved by strychnine. When failing compensation sets in, the usual treatment of rest and cardiac tonics is to be employed, and here strychnine is said to give better results than digitalis.

Thus, in a very few words, a careful hygiene and an expectant and preventive treatment may be summed up as the only available assistance that can be given. The condition does not admit of cure, but permits of amelioration and of arrest of the downward trend of the disease.

¹ *Ann. Surg.*, 1907, xlvii, 335.

DUE DATE

ES

e	APR 5	1994	APR 26 1994	t the
p				g, as
n				nge-
DA				
	201-6503		Printed in USA	

1139
ON PERSONAL RESERVE SHELF.

7128

AUG 6 1958

W. Z. Hyman
N. Leach
8-17-58 Rem

1-1-59
JAN 25 1959

RC683

Ab2

COLUMBIA UNIVERSITY LIBRARIES



0037552694

